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MANAGEMENT OF ULCERS AMONG NAVAL PERSONNEL*

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AND

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GASTRO-INTESTINAL DISEASE constitutes a major problem among military personnel. Of more than 3,564 patients with dyspepsia, admitted to military hospitals in Great Britain, 55 per cent were found to have peptic ulcer. These figures include some reported from Naval hospitals. In the United States Army, in 1940, diseases of the digestive system ranked third as a cause for admission to sick report; fourth as a cause of death; and fifth as a cause of discharge for disability.[7] Of all medical patients admitted to a general hospital of the United States Army, 18 per cent had symptoms of digestive disease.[10]

In spite of the statistics from Great Britain (Table I) and this country, there is little evidence to suggest an increase in peptic ulcer as a result of the present war but, as has been pointed out,[2] the war certainly has revealed the unexpected frequency of peptic ulcer in the civilian population before the war began. Several authors[4, 6] have found that about 90 per cent of the soldiers with peptic ulcer in the Army of the United States had had ulcer prior to entering the service. The seriousness of this problem is attested by the fact that in one report[2] it is stated that 90 per cent of the patients with ulcer were discharged from the British Army. A similar report[13] stated that about 50 per cent were invalided from the Royal Navy. As yet, we have no data on the influence of combat on the production of ulcer in our services.

Certainly many physicians will agree that under proper conditions patients who have peptic ulcer are capable of performing many important tasks, even though such duty may be limited. If these patients cannot tolerate the army or navy ration without recurrence of symptoms, they are promptly invalided from the service.[3] Flood[4] has stressed the fact that soldiers with peptic ulcer who are retained in the army should be of stable personality, because those with a neurotic temperament fare badly.

In the navy, since highly trained men are such a valuable asset, manage-

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† On leave of absence from the Mayo Clinic.

ment of the patient with peptic ulcer, with the thought of returning him to duty, cannot be overemphasized. The evidence is ample that peptic ulcer is a difficult problem in the naval service, especially aboard ships, because naval service affords little opportunity for the physiologic gastroduodenal rest that is the essential part of the nonsurgical treatment of ulcer. Every ocean voyager knows of the hypermotility and hypersecretory action of the stomach and duodenum which are called seasickness. In most instances symptoms of ulcer without complications among new recruits in the navy were present prior to enlistment. Since most of these men are young (from 18 to 25 years of age), few in his group should be considered as candidates for surgical procedures. Hence, experience has shown that it is advisable to discharge such men from the service before six months* have elapsed from their enlistment, or the government becomes responsible for their continuous treatment and disability pensions.

On the other hand, officers and enlisted men whose ulcers have developed during their period of active duty are entitled to pensions and continuous medical or surgical treatment. Should they, too, be retired or be invalided from the service because of their ulcers? The indications for operation differ little in these cases from those in cases in civilian life. There seems to be an impression in the naval service that even if such patients are operated upon most of them will have to be assigned to shore duty (limited duty). This requires that an officer first be retired from active service and then recalled as a retired officer for limited duty. We believe, on the contrary, that a large majority of these patients who have active, chronic or recurring ulcers may be returned to active duty at sea or foreign stations even in the combat zones of operation, preferably partial gastrectomy, is performed as soon as the diagnosis is established. Consequently we have operated upon a selected group of those encountered at a base hospital in the last six months and returned most of them to active duty for a therapeutic trial. This, therefore, is essentially a preliminary report since we have operated upon only thirteen such patients in the past six months. Although eleven (85 per cent) have returned to active duty, it will be necessary to have a series of at least 100 cases, and to follow these for a year or more, before any definite decision can be arrived at concerning the results of the operation from the standpoint of the ability of the patient to perform active duty as a part of the navy after operation.

REPORTS FROM THIRTEEN UNITED STATES NAVAL HOSPITALS

In order to broaden the scope of the preliminary report, we have sought information from many of the larger naval hospitals in this country to determine the attitude of other medical officers on the ulcer problem among naval personnel. Special emphasis was placed on the percentage of patients thought to have a lesion requiring surgical measures, the operation performed, and the subsequent clinical course.

* Recently changed to three months.

TABLE I

INCIDENCE OF PEPTIC ULCERS AMONG BRITISH MILITARY AND NAVAL PERSONNEL ADMITTED TO HOSPITALS BECAUSE OF DYSPEPSIA

Authors	Type of Hospital	Total Cases	Peptic Ulcers, Per Cent	Gastric Ulcers, Cases	Duodenal Ulcer Cases	Per Cent of Gastric and Duodenal Ulcers
Wade	Naval	1003	47	67	404	86
Brockbank*	Military	931	42.5	52	275	84
Morris	Military	500	50	..	....	.
Payne and Newman	Army	287	89	42	164	80
Maingot	General	256	56	15	128	89
Graham and Kerr	Military	246	64.3	20	135	85
Spillane	Military	200+	32	10	54	84
Allison and Thomas	Naval	100	45	6	34	85
Wilcox	General	41	69	7	19	73
		Total—3564	55	219	1213	85

* Includes one case of carcinoma and nine of gastro-enterostomy, in which there was no precise evidence of the site of ulcer.

TABLE II

TYPE AND TREATMENT OF PEPTIC ULCER
(*Collected Series*)

Type of Ulcer	Total	Treatment, Cases	
		Surgical	Medical
Gastric	112	23	89
Duodenal	1219	72	1147
Gastric and duodenal	21	8	13
Total	1352	103	1249

TABLE III

DISPOSITION OF PATIENTS WITH ULCER AFTER TREATMENT
(*Collected Series*)

Disposition	Total	Surgical Patients	Medical Patients
Active duty	654	53	601
Limited duty	131	20	111
Discharged*	567	30	537
Total	1352	103	1249

* Of the total number listed as discharged, and retired from service, 137 had actually been transferred for further disposition, two were still under treatment, and three had died.

We have had reports of 1,352 patients with proved peptic ulcer who entered thirteen United States naval hospitals from December 1, 1940, to December 1, 1942 (Table II).* One thousand two hundred and forty-nine

* The cooperation of the following commanding officers and their associates is greatly appreciated. The information collected by them and their suggestions have been freely used in this paper: U. S. Naval Hospital, Portsmouth, New Hampshire, J. T. Bennett; Pensacola, Florida, W. W. Hargrave and L. M. Nelson; Newport, Rhode Island, G. F. Thomas; Quantico, Virginia, P. M. Albright and W. M. Sheppe; Long Beach, California, L. D. Powell; Seattle, Washington, F. F. Murdock; Key West, Florida, J. W. Allen; Chelsea, Massachusetts, G. F. Clark and G. E. Cummings; Norman, Oklahoma, L. B. Marshall; National Naval Medical Center, Bethesda, Maryland, John Harper and W. T. Gibb, Jr.; Balboa, Canal Zone, The Commanding Officer; Pearl Harbor, T. H., J. J. A. McMullin and C. E. Watts; Portsmouth, Virginia, Daniel Hunt and Michael Lake; Corpus Christi, Texas, R. R. Gasser; Mare Island, California, J. P. Owen and E. L. Markthaler; Corona, California, H. L. Jensen.

TABLE IV

SURGICAL TREATMENT
(*Collected Series*)

Operation	Total
Resection with Pólya-type of anastomosis	39
Billroth-I resection	8
Gastro-enterostomy	8
Local excision	12
Other types*	36*
Total	103

* Most of these are closures of acute perforations.

TABLE V

NUMBER AND DISPOSITION OF PATIENTS PREVIOUSLY OPERATED UPON FOR PEPTIC ULCER WHO ENTERED HOSPITAL WITH RECURRENT ULCER OR OBSTRUCTION

Type of Treatment	Cases
Surgical	16
Medical	47
Total	63
Disposition	
Active duty	18
Limited duty	6
Discharged*	39
Total	63

* Of the number discharged, one died.

(92 per cent) of these patients were treated medically and 103 (eight per cent) surgically. Seventy-one per cent of the 103 patients treated surgically were returned to duty; 53 to active, and 20 to limited duty (Table III). Fifty-five per cent of those treated medically were returned to duty. In about half of the surgical cases partial gastrectomy was performed, and in approximately a third simple closure of an acutely perforated ulcer was employed (Table IV). Of the 63 patients who had had previous operations for ulcer, 25 per cent underwent another operation for recurring ulceration, with or without obstruction. Seventy-five per cent were treated medically. Thirty-eight per cent of these 63 patients were returned to duty (Table V). Ninety per cent of the 1,352 patients had duodenal ulcers, eight per cent gastric ulcers, and two per cent gastric and duodenal ulcers. The high percentage of duodenal ulcers (90 per cent) is in accord with the average 85 per cent reported by current British writers (Table I).

In the collected series from the United States naval hospitals, the reasons generally listed for discharging patients treated surgically from the service was their inability to tolerate a general diet. Of those treated medically, and later discharged, the reasons were listed as follows: (1) Disease existed prior to enlistment (E.P.T.E.) in a young recruit; (2) history of many recurrences; (3) symptoms not relieved and surgical intervention refused; (4) repeated hemorrhages; and (5) accompanying severe functional disturbances.

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Surgical Measures.—The reasons for choosing surgical treatment for naval patients with peptic ulcer are essentially the same as those for civilian

patients. In our series of 13 cases surgical treatment was advised for (1) repeated hemorrhages; (2) pyloric obstruction; (3) perforation; or (4) frequent recurrences, with progressive symptoms in spite of medical treatment. Partial gastrectomy, with a posterior Pólya-type of anastomosis, was performed in 85 per cent of the cases; in one case gastro-enterostomy was performed because technical difficulties prevented gastric resection; in one case of perforated duodenal ulcer simple closure was, at the time, the procedure of choice.

The importance of making an early decision as to the type of treatment to be employed and the disposition of the patient cannot be overemphasized. If surgical treatment is indicated, the earlier the operation is performed and the patient returned to duty, the better. Since all these patients are hospitalized, there is a tendency to delay this decision until the patient has become so accustomed to hospitalization that he is reluctant to return to combat duty, regardless of the result of treatment. In our group of 13 cases in which operation was performed, only two patients were invalided from the service. One was an officer who had spent a total of 14 months in various hospitals undergoing several courses of medical treatment before operation was advised. Although the surgical result was physiologically and clinically excellent, the long period away from duty and the mental attitude developed by prolonged hospitalization and limitation of activities both physical and dietary were sufficient to produce a functional failure in two months after his return to active duty. The second patient had a good result from operation, but was discharged because of an incapacitating war injury.

Medical Measures.—The medical treatment of peptic ulcer in the navy is essentially the same as that employed in civil practice, but the various duties to which the naval personnel are assigned after leaving the hospital make this nonsurgical form of treatment difficult. Irregular hours, inadequate meals, seasickness, great exertion, great fatigue, and the nervous strain and apprehension over real and impending battle are a great hindrance to medical management. Medical treatment, therefore, is advised only when symptoms are extremely mild and of short duration, and complications are not present.

Aboard large ships, because of special messes and privileges, officers who have ulcers have a better opportunity for adequate medical management than enlisted men do. For this reason every opportunity is given them to return to duty if their ulcer is responsive to the usual treatment; if it is not responsive surgical intervention is advised. We have observed 35 patients with proved gastric or duodenal ulcer at a naval base hospital in this country during the past six months. Twenty-two were treated medically; 16 (73 per cent) of these were returned to duty and six discharged. Of the six discharged, three were advised to have operations because of complications, but refused; the other three had medical conditions other than ulcer requiring discharge.

Our patients with ulcer have cooperated well, and almost all have been anxious to return to duty. Those who responded to medical treatment did

so in the manner usually expected in civilian practice. This is in contrast to the experience of Flood, who observed that in the army, a large number of patients continued to complain of discomfort even after long periods of adequate treatment. Many of our patients have experienced dangerous and strenuous action, and date their gastro-intestinal symptoms from that period of mental and physical stress and strain. A large percentage of these patients quickly become free of symptoms, simply with rest and proper food at regular intervals. Those who lose their symptoms quickly and evidence desire to return to duty are returned without restrictions; others, less sure of themselves, who experience occasional dyspepsia are returned to limited duty ashore; those who have serious complications are advised to have an operation. Time and experience will determine the success of this policy but in view of the increasing need of trained manpower this program seems justified.

FURTHER STUDIES ON THE ULCER PROBLEM

It is fairly obvious that further study of treatment of ulcer among men in the navy is indicated. At present, we are not concerned with young recruits who have ulcers that existed prior to enlistment (E.P.T.E.). Such patients are discharged from the service because medical treatment cannot be carried on with any degree of satisfaction and yet they do not have sufficient trouble so that surgical procedures can be advised. When the ulcer is incurred during the period of the active service, however, it is important to treat the patient in such a way that he may return to duty if possible. This is particularly important if the patient is an officer, or a specialist who has become a real asset to the service.

Several problems must be solved in these cases: The first is whether repeated medical treatment is advisable. Of 537 patients in the collected series medically treated and discharged from service because of ulcer, 25 per cent had repeated periods of hospital treatment for their ulcer. The chances of those in this group of responding to medical treatment so that they become useful to the service is exceedingly doubtful. The second problem is the need of follow-up studies to determine the results of surgical treatment in the naval service. In our series, 37 per cent of the patients were treated surgically, 85 per cent of whom we returned to duty. In the collected series, only eight per cent were treated surgically, of whom 71 per cent were returned to duty. These results should be compared with those of conservative medical treatment. Seventy-three per cent of the patients in our series treated by medical measures only and 55 per cent of the patients in the combined series treated by medical means, returned to duty. These figures suggest that surgical treatment, when indicated, deserves wider use.

As previously mentioned, 25 per cent of the patients treated medically who were discharged from the service had been hospitalized repeatedly because of ulcer. It seems possible that surgical treatment should be employed more extensively in this group of cases.

To evaluate the final results of surgical treatment will require a follow-up study to determine (1) the time spent on the sick list; (2) ability to stand active and limited duty; and (3) a comparison of both medically treated and surgically treated patients to determine whether the radical treatment by gastric resection is warranted.

Certainly, from the results shown herein, there is, we believe, justification for radical surgical treatment of naval patients who have chronic, recurring, gastric or duodenal ulcers which develop during service. Officers and enlisted specialists with such ulcers, whose knowledge, experience and ability in naval activities make them particularly valuable to the navy, and the 25 per cent of medically treated patients who are discharged from the service because of chronic recurring ulcers, are the particular patients, we believe, that should be given the benefits of surgical treatment with the hope and expectation that their valuable services can be retained. However, until a much larger series of naval patients are operated upon, and observed subsequently as regards their reaction to naval duty, the advisability of surgical treatment of naval personnel who have gastric and duodenal ulcers in order to return the patients to duty cannot be determined definitely.

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DISCUSSION.—COLONEL ROBERT H. KENNEDY, M.C. (New York): My commanding officer, up to a recent time, General Kirk, was extremely regretful that he could not be here. At the time that the preliminary program was received he asked our Chief of Gastro-Intestinal Section to prepare some data relevant to the paper of Captain Walters, and since he went away he wrote asking me to assemble this material and discuss the subject in his absence. This was prepared by Major Charles M. Caravati.

At the Percy Jones General Hospital, between January 15 and May 1, 1943 (the hospital opened on January 15) there have been 835 total medical admissions, of whom 69 were peptic ulcer patients.

Admitted to the Gastro-Intestinal Service were 108, 58 of whom were proven ulcers on that service. There were 11 more ulcers on the officers' ward (Table I).

TABLE I

THE ULCER PROBLEM AT PERCY JONES GENERAL HOSPITAL
(*January 15 to May 1, 1943*)

	No. of Cases
Total medical admissions	835
Total number of peptic ulcer patients	69
Total admissions to G. I. Service	108
Total proven ulcers on G. I. Service	58
Total admissions to Medical Officers Ward	125
Total proven ulcers on Medical Officers Ward	11

The diagnosis has been accepted by an attempt to follow the following criteria:

1. Careful perusal of the clinical story.
2. Complete roentgenologic studies, with repeat examinations when indicated.
3. Gastric secretory studies, including night acid curves.
4. Examination of three specimens of stool for occult blood.
5. Critical review of the psychic status of the patient.
6. Response to therapy.
7. Gastroscopic examination.

(1) *Clinical History:* There were only a small percentage of patients in which the clinical history was not at least suggestive of peptic ulcer, who were later proved to have ulcer. However, in three individuals, the finding of a definite ulcer crater, which disappeared under treatment, was demonstrated though the history, in no way pointed to the presence of same. Ninety to 95 per cent of soldiers proven to have ulcers gave a history suspicious of same existing prior to entrance into the service. This agrees with reports of other army hospitals—Chamberlain of Lawson General, reporting 90 per cent; Thomas of Fort Meade Station Hospital, 93 per cent, and Berk at Tilton General, approximately 90 per cent. Eight cases had had a history of acute perforations. Eight had gross but not massive gastro-intestinal hemorrhages. None of these were admitted during the acute stage of their hemorrhages. There was only one case of gastric ulcer in this series. Other series, in the Army and Navy, have reported an incidence of four to eight per cent of all peptic ulcers occurring within the stomach. Fifty-two of the 69 soldiers with ulcer, had seen overseas service. Ninety per cent of these gave histories indicative of the presence of ulcer prior to their entrance into the Army. The one case of perforation which occurred on our service had returned from overseas eight days previously.

(2) *Roentgenologic Examination:* In a small percentage of cases, clinical evidence and the roentgenologic findings did not agree. At times the clinician expected a roentgenologic report of duodenal deformity when the Roentgenological Department reported negative findings. The variability of the roentgenologic evidence of ulcer was forcefully pointed out in an analysis of some of these cases. The presence of a crater, with deformity, was considered definite evidence of an ulcer, usually active. Deformity, without a crater, but with a niche, or marked duodenal irritability, also was considered to indicate probable presence of an ulcer. Absence of irritability, with the presence of deformity, and with the absence of subjective symptoms, was most often interpreted as a probable healed ulcer.

(3) *Gastric Secretory Study:* Study of gastric secretion was accepted, using three methods:

(a) Quantitative study of the basal secretion.

(b) A study of the acid curve after alcohol stimulation, and after histamine, when there was no free acid after oral alcohol.

(c) Study of the night acid curve (aspirations every two hours).

A study of the gastric secretion of this group, using alcohol as a secretory stimulus, reveals that there appears to be less hypersecretion in this group than in most cases reported from civilian life. It has been formerly taught that the free acid level is usually

higher in this age-group than in a comparatively older group, and in this series of cases, over 50 per cent of the proven cases of ulcer showed normal acidity curves.

(4) *Occult Blood in Stool:* It is regrettable that, due to faulty laboratory technic, our findings are probably incorrect. In no case was the presence of occult blood reported positive before April 15th, but since that time several cases have been positive, after a change in technical procedure was adopted in the laboratory.

(5) *Psychic Study:* A critical review of the psychogenic status of each patient indicated that a marked neurogenic element was present in a very large percentage of soldiers with duodenal ulcer. Psychic trauma often appeared to act as a "trigger" mechanism, apparently reactivating a dormant lesion. It was the opinion of most observers that activation of the epigastric distress which was prominent in many soldiers returning from overseas to the mainland, and which was not apparently related to seasickness, was best explained on the basis of anxiety, incident to the hazardous sea voyage through heavily submarine-infested waters. The diet did not impress us as being unsatisfactory.

(6) *Response to Therapy:* Conservative medical management consisting of an adequate, bland, low roughage diet, with frequent interval feedings made up chiefly of milk, crackers and juices, was adhered to in all cases except the very acute. In the latter group, which comprised only a few patients, they were placed in bed and given milk and cream at two-hour intervals during the 24 hours, with aluminum hydroxide frequently. All other cases were treated ambulatory, except two with pyloric obstruction, in which Wangensteen suction and aluminum hydroxide drip were used alternately. Each patient was given ascorbic acid 100–200 mg. t. i. d. Tincture of belladonna was administered to all in whom there appeared to be evidence of hypertonus. Several patients were placed solely on olive oil.

Results: Regardless of the routine followed, all patients reacted uniformly well to simple but intense medical management. The average length of time from admission, to relief of symptoms was less than four days. Many were relieved within 24 hours. No case of proven uncomplicated ulcer failed to receive relief within ten days under management as above described, except one who had an acute perforation while under a milk and cream regimen, and was bedfast.

(7) *Gastroscopic Examination:* Twenty-five returned overseas soldiers with duodenal ulcers were gastroscoped; six showing positive findings. Five of these represented gastritis, and one edema. Of those showing gastritis, four were of the superficial type and one of the atrophic type. All were very mild, in fact, it was the impression of the Endoscopists that in only one of these cases was the pathologic change sufficient to cause clinical symptoms. These examinations were conducted without previous aspiration of the stomach, in order to eliminate the factor of trauma from the interpretation of the findings.

The positive diagnosis of ulcer now requires that a soldier be separated from the Service, except in the case of married officers, who may be recommended for limited duty if they can be stationed at a post where they may live at home and follow a satisfactory dietary regimen as ordered.

CAPTAIN WALTMAN WALTERS, M.C., U.S.N.R. (closing): I should just like to say a word, in closing, regarding the large number of men who are being discharged from the armed forces because of chronic gastric and duodenal ulcer. As I said in my paper, there certainly is no indication to operate upon young men of 18 to 25 years of age who have had symptoms which existed prior to enlistment. Most of these men do not have complications unless they perforate, which few of them do.

On the other hand, from my reasoning, I can see no reason why, if the operation of partial gastrectomy has given the excellent results that it has in patients with surgical ulcers who required operation for several years, such results cannot be expected when a similar type of operation is performed under similar indications upon men, and valuable men, in the armed forces, and that is a particular reason why Doctor Butt and I were carrying on this study.

The need for such a study is emphasized by the fact, also, that in this collected series of 1352 patients with proven ulcer reported, from several Naval hospitals, in only eight

per cent of those cases had surgical procedures been carried out. Yet, in the very small group of cases which we reported, we carried out surgical procedures in 37 per cent of the cases.

Now, there is only one way that one is going to determine whether or not a surgical procedure is advisable in Naval personnel who have surgical ulcers, and that is to perform a sufficient number of operations upon a sufficient number of patients in whom surgical treatment is indicated, and give them therapeutic trial duty, at home and abroad, and see what the results are. I, personally, believe that it will show that about the same results can be expected as obtain in similar operations upon civilians, namely, that probably 80 per cent of those patients can eat anything and do anything, and that is one particular reason for this paper.

EFFECTS OF PEDICLE GRAFTS OF JEJUNUM IN THE WALL OF THE STOMACH ON GASTRIC SECRETION*

Experimental and Clinical Studies

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Experiments which have been carried out in our laboratory have revealed the fact that when a pedicle graft of jejunum is implanted in the wall of the stomach profound effects are produced on gastric secretion.[1, 2, 3] It is with such effects and their possible employment in the treatment of peptic ulcer that this paper deals.

Methods.—Healthy mongrel dogs were used for these experiments which consisted in the resection under nembutal anesthesia of an area of the anterior wall of the stomach approximately 4 x 6 cm. in size and about midway between the cardia and pylorus, and the implantation into this defect of a pedicle graft of upper jejunum with its circulation intact. This was obtained by isolating a segment six centimeters in length which was then opened along its antemesenteric border and fastened in place by means of interrupted sutures of silk. The continuity of the jejunum was restored by end-to-end suture.

The gastric secretion of each animal had been examined after 24 hours' fast at least once before the beginning of the experiment. In the first few animals the gastric analyses were carried out under light nembutal anesthesia, but this was found to be unnecessary and, although it appeared to have no appreciable effect on the secretion, was abandoned for simple analysis using animals trained to tolerate a small stomach tube. At the time of operation direct measurements of the p_H of the surface of the mucosa at seven different areas in the stomach were made by inserting electrodes of the Beckman p_H meter through the defect in the anterior wall just prior to the implantation of the jejunal graft. Subsequent analyses were carried out in a similar fashion and p_H determinations were made from 45 minutes to two years and six months after the implantations, inserting the instrument through a gastrotomy.

Control animals were subjected to anesthesia and operations of similar length, as well as to resection of an area of the gastric wall and closure of the defect without a graft.

Twenty-five animals subjected to this procedure, in one form or another

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have been studied, 19 having had gastric analyses, 13 p_H measurements, and six being investigated by both methods. A summary of the results is set forth in Figures 1 and 2. Of the 13 animals in which the p_H studies were carried out after the implantation of a jejunal graft, 12 showed a rise in the average hydrogen ion concentration of seven regions of the gastric

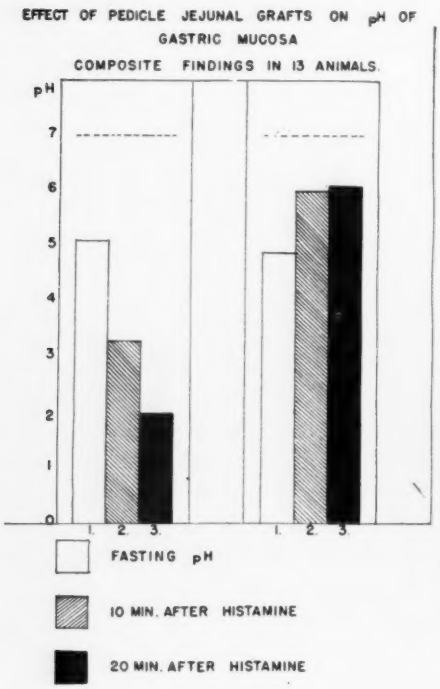

FIG. 1

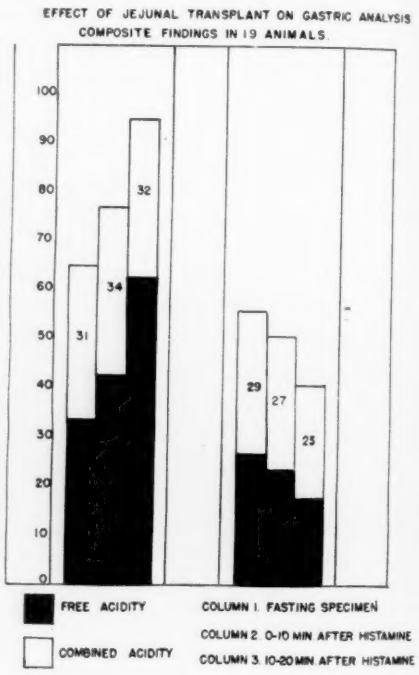

FIG. 2

FIG. 1.—Effect of pedicle jejunal grafts on p_H of gastric mucosa.
FIG. 2.—Effect of jejunal transplant on gastric analysis.

mucosa following the administration of histamine in contrast to the findings before operation. In the remaining animal this reversal did not occur, but the fasting p_H was 6.7 compared to a preoperative level of 5.4 and the fall after histamine was considerably less marked.

In the group of 19 animals in which gastric analyses were performed the average fasting free and total acidity was definitely lowered after operation and following the injection of histamine these values declined progressively in 17. In one of the remainder the rise after histamine was comparatively small and the p_H studies of the gastric mucosa were at variance with the gastric analysis—the former showing a definite rise of p_H. In only one animal was there evidence of increased acidity after histamine, in both the gastric analyses and p_H studies following operation. When the graft in this dog was investigated it was found to be the seat of circulatory disturbances, the mucosa being markedly congested and superficially ulcerated.

There were numerous adhesions about the pedicle. This graft, the only one by the way to show such disturbances, was resected and a fresh graft implanted, following which the usual findings after jejunal graft supervened.

While this animal is included in the series summarized in Figures 1 and 2, the result was a decided exception, and, inasmuch as it was corrected by reoperation, seems to have been due to an error in technic. It does serve to emphasize, however, the need for most meticulous regard for the circulation of the graft when it is implanted.

It appears, therefore, that in these animals the implantation of pedicle jejunal grafts in the wall of the stomach has tended to lower the fasting acidity and has reversed or considerably diminished the normal rise in acidity following the injection of histamine. In all but one instance in which the average p_H of seven regions of the gastric mucosa was studied the normal fall in p_H following histamine was converted into a rise in this value.

As to the time of their development, these changes vary somewhat even in the experimental animals, the p_H changes coming on in some as early as 45 minutes after implantation of the graft, while in others, for no apparent reason, these as well as the alterations in acidity in the gastric analysis may be delayed for several weeks. The alterations persist for as long as we have kept animals, which is now more than two and one-half years.

In two dogs, when the effects of the transplant were established, it was then resected and further p_H measurements carried out. These indicated that within one hour one animal showed the normal response to histamine, although the fasting p_H remained slightly higher than before the graft was implanted. In the other the p_H of the gastric mucosa and its reaction to histamine corresponded to the normal findings in all respects.

In order to compare the reaction of the animals subjected to this operation to some secretory stimulus other than histamine injected intramuscularly, a modification of the method of Bloomfield and Keefer,[4] employing alcohol as the secretogogue, was used.

Method.—Dogs of both sexes were used after having received no food for 24 hours. Following the aspiration of a fasting specimen of gastric juice, 50 cc. of seven per cent alcohol was administered and allowed to remain in the stomach for ten minutes. The entire contents of the stomach was then aspirated; 20 cc. was withheld and the remainder replaced in the stomach. Ten and 20 minutes later the same procedure was repeated. All specimens were titrated with 0.1 normal NaOH in the usual manner.

In Figure 3 the results of this test in five normal animals are compared with those in seven with pedicle jejunal grafts. It will be seen that the marked increase in acidity which followed the instillation of alcohol in the controls is almost completely lacking after the implantation of pedicle jejunal grafts.

Having established the fact that pedicle grafts of jejunum produce these effects, the question quite naturally arises as to whether grafts from

other levels of the tract possess similar properties. A series of animals were, therefore, assembled, three with transplants from the transverse colon, three with ileal, four with duodenal and five with jejunal grafts; and the gastric analyses and mucosal p_H after histamine compared with those in five normal animals. These studies indicate that the property of depressing gastric acidity is confined to grafts from the jejunum and duodenum with the former possessing somewhat greater activity (Figs. 4 and 5).

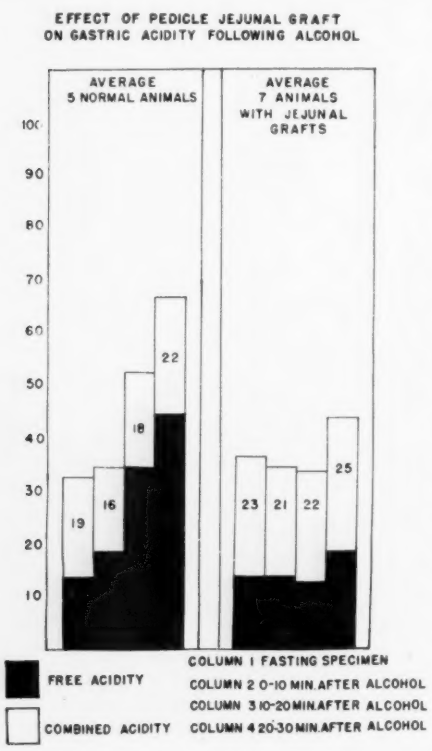

FIG. 3.—Effect of pedicle jejunal graft on gastric acidity following alcohol.

Since gastro-enterostomy is so frequently effective in relieving symptoms of peptic ulcer, it would seem important to compare the secretory effects of this operation with those following implantations of a pedicle jejunal graft. To this end, the following series of experiments were carried out.

After preliminary gastric analyses, six dogs were operated upon and the response of the p_H of the gastric mucosa to histamine determined in the manner described above. Following this, an anterior gastro-enterostomy was performed and a period of from one to three weeks permitted to elapse, at the end of which time these determinations were repeated. The bowel about the gastro-enterostomy stoma was then converted to a pedicle graft by dividing the jejunum approximately two centimeters proximal and distal, and inverting toward the stoma beneath mattress sutures of medium silk. The continuity of the intestine was then reestablished by end-to-end anastomosis.

The results of these experiments are shown in Figures 6 and 7. In each instance, gastro-enterostomy failed to modify materially the response to histamine as it appeared in the gastric analysis, whereas, after the conversion of the bowel about the stoma to a pedicle graft the histamine response was reversed in all animals and the fasting free acidity markedly lowered in all but one.

In five out of six, gastro-enterostomy failed to prevent a marked diminution of the average p_H of the mucosa of seven different regions of the stomach after histamine, but following conversion to a pedicle graft the p_H rose progressively when histamine was administered.

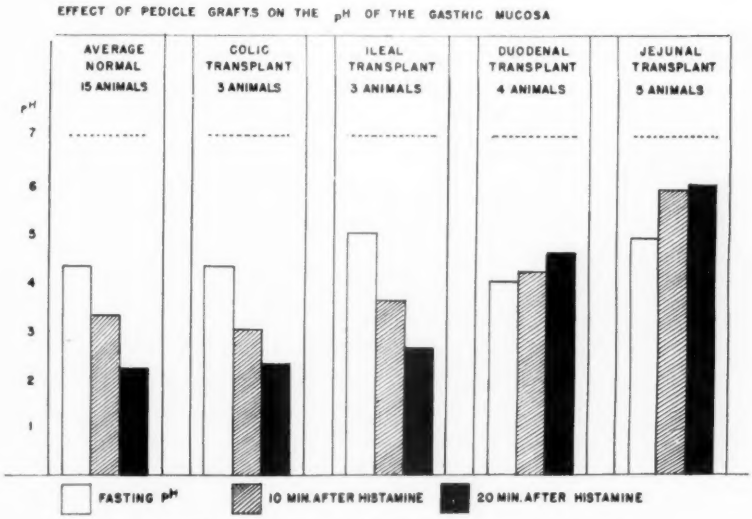

FIG. 4.—Effect of pedicle grafts on *p*H of the gastric mucosa.

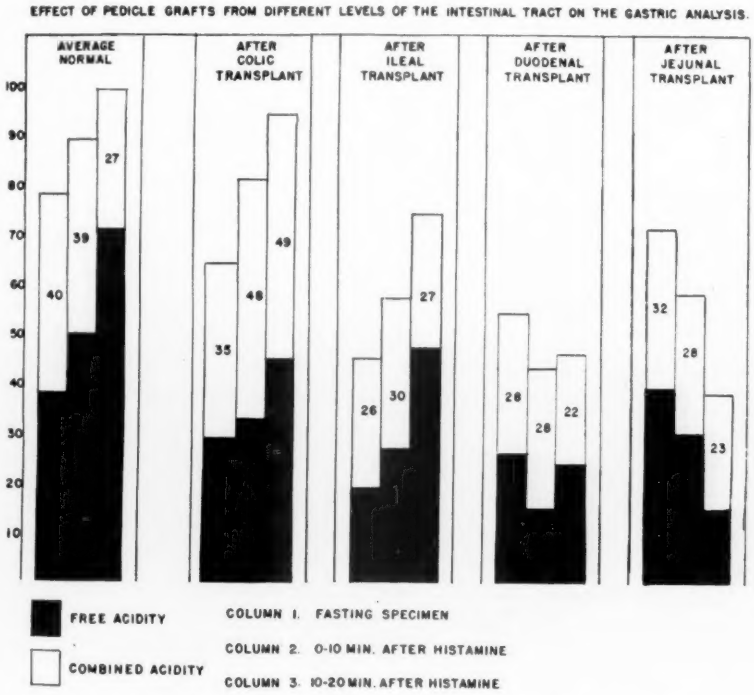

FIG. 5.—Effect of pedicle grafts from different levels of the intestinal tract on the gastric analysis.

The results cited above have led us to postulate the presence in the jejunum of a substance which, when introduced into the lumen of the stomach, depresses the acidity of the gastric juice. Although such a substance has not yet been identified, evidence of its presence in washings of isolated jejunal loops has been obtained in the following experiments.

In five dogs, a segment of jejunum was isolated as for a pedicle graft, but instead of being opened and implanted in the wall of the stomach, one end of the segment was inverted under mattress sutures and the other end brought out through a stab wound at one side of the celiotomy incision. In three animals, the segment was approximately six centimeters in length while in two it measured 12–15 cm. The continuity of the intestinal tract was reestablished by end-to-end anastomosis.

After at least two weeks had elapsed to allow for healing, these loops were washed out two or three times with 25 cc. of normal saline and the washings collected. To study the effects of such washings on gastric secretion the following technic was employed.

TABLE I

EFFECT OF WASHINGS OF ISOLATED JEJUNAL LOOPS ON GASTRIC SECRETIONS

	I. Experimental Series						II. Normal Control Series						III. Saline Control Series					
	Fasting		0-10 min. after Hist.		10-20 min. after Hist.		Fasting		0-10 min. after Hist.		10-20 min. after Hist.		Fasting		0-10 min. after Hist.		10-20 min. after Hist.	
Gastric Analysis	Vol.	32°F	Vol.	8°F	Vol.	33°F	Vol.	31°F	Vol.	40°F	Vol.	67°F	Vol.	21°F	Vol.	38°F	Vol.	74°F
	12 cc	25°C 57°T	12 cc	20°C 28°T	17 cc	24°C 57°T	15 cc	32°C 53°T	11 cc	34°C 74°T	15 cc	27°C 94°T	11.4 cc	24°C 45°T	18 cc	21°C 59°T	23 cc	20°C 94°T
mgm. HCl.	24.96		12.26		35.37		29.02		29.71		51.46		18.72		38.76		78.91	
mgm. HCl. cc	2.08		1.02		2.08		1.94		2.70		2.43		1.64		2.15		3.41	
Parietal Secretion	4.16		2.04		5.90		4.64		4.96		8.58		3.12		6.46		13.15	
NonParietal Secretion	7.84		9.96		11.10		10.36		6.05		6.42		8.28		11.54		9.85	

I. Average Values in 15 Animals.
II. " " " 8 "
III. " " " 8 "

Normal dogs which had had at least one previous gastric analysis and which had been trained to tolerate a small stomach tube were used as subjects, having been without food for 24 hours. After collecting the normal fasting secretion during a period of ten minutes the entire 25 cc. of jejunal washings was instilled into the stomach and allowed to remain for ten minutes when it was removed, together with the gastric secretion during this period. At this point, the dog received the usual one milligram of histamine intramuscularly, and further specimens representing the secretory response over ten-minute periods were collected.

Two of the animals, Nos. 1925 and 2072, received the washings from all five donor animals at different times, while the other three were used to test the material from one or more loops. In all, 15 tests designated in Table I as Series I were made in the five recipient animals.

The jejunal washings were found to be of p_H 5.9 to 6.5, and to contain practically no titratable buffer, as the p_H was altered by three points when one drop of N/10 HCl or N/10 NaOH was added to five cubic centimeters of the washings.

As controls, eight animals, Series II, including the five used as recipients in the experiments, were subjected to one or more routine gastric analyses, and additional analyses, Series III, exactly comparable to those used to test the jejunal washings except that saline alone was instilled, were carried out in eight animals, including Nos. 1925 and 2072 of the experimental series.

While the specimen removed at the end of the ten-minute period during which the jejunal washings remained in the stomach always showed a marked reduction in acidity, it seemed possible that the factor of dilution with an indeterminate portion of the 25 cc. of material instilled might have influenced the result, and for the comparison with the control series this specimen was, therefore, discarded.

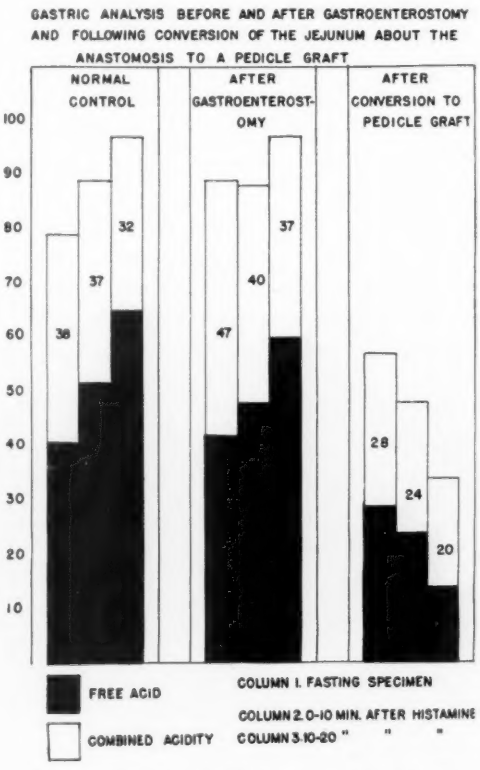

FIG. 6.—Gastric analysis before and after gastroenterostomy and following conversion of the jejunum about the anastomosis to a pedicle graft.

The comparative results in the experimental and control series appear in Table I. From these figures it is apparent that while the injection of one milligram of histamine is followed by a considerable rise in both the free and total acidities in both of the control series, there is a definite fall in each of these values when the injection follows the instillation into the stomach of washings of isolated jejunal loops. By the end of 20 minutes the effect of the instillation has worn off to some extent (Fig. 6).

Recognizing that the facts so far presented indicate that pedicle jejunal grafts exert definite effects in lowering qualitatively the acidity of the gastric secretion, it remains to be shown whether the reduction is also quantitative, and whether the effects are produced through neutralization of gastric juice or actual inhibition of secretion. Evidence bearing on these points is available from several sources: First, the data on the p_H of the gastric mucosa indicate inhibition rather than neutralization, particularly since it can be

demonstrated that the changes take place even when the pylorus is completely obstructed. The same impression is gained by noting in the gastric analysis the total milligrams of acid secreted and the concentration per cubic centimeter. Reference to Table II, containing the data concerning the gastric secretion in ten typical experiments, shows that the total amount of HCl. secreted, which normally increases considerably following the administration of histamine, remains at or below the fasting level in animals with jejunal grafts. Obviously, the concentration of acid as measured in milligrams per cubic centimeter follows the figures for the total acidity.

TABLE II

GASTRIC SECRETORY FINDINGS BEFORE AND AFTER IMPLANTATION OF PEDICLE JEJUNAL GRAFT: COMPLETE DATA IN TEN CONSECUTIVE EXPERIMENTS

	Before Operation									After Operation								
	Vol.	Fasting		Vol.	0-10 min. after Hist.		Vol.	10-20 min. after Hist.		Vol.	Fasting		Vol.	0-10 min. after Hist.		Vol.	10-20 min. after Hist.	
ANIMAL NO.	c.c.	F.	T.	c.c.	F.	T.	c.c.	F.	T.	c.c.	F.	T.	c.c.	F.	T.	c.c.	F.	T.
1909	5	60	90	8	72	106	13	80	108	7	28	58	10	22	52	6	10	38
1917	4	45	105	9	60	110	10	64	116	8	24	44	10	20	40	5	4	22
1934	6	38	80	5	42	86	12	56	96	12	26	64	5.8	26	64	6	12	48
2013	18	40	68	22	52	82	19	76	96	10	34	54	16	30	46	22	32	44
1986	12	20	48	19	52	60	14	50	72	13	32	64	21	20	30	29	10	16
2115	19	22	38	14	32	48	26	64	82	5	0	16	8	0	12	24.5	2	12
2106	5	0	14	7	2	18	16	38	60	37	18	38	14	12	34	9	8	32
2077	11	16	28	15	14	40	12	40	78	25	40	66	18	44	70	36	32	54
2119	55	38	58	30	0	18	25	44	62	8	22	60	26	20	56	31	20	50
2161	19	46	80	16	64	94	29	88	104	17	40	66	13	0	6	18	0	4
Averages	12.7	32.5	60.6	14.5	37	66.2	17.6	58.9	87.4	13.9	26.4	55	14.2	19.6	41	18.5	13	31.8

Following Figures are Derived from Averages of Above Ten Animals

mgm. HCl.	28.11	35.04	56.14	26.90	21.24	21.46
mgm. HCl./cc	2.21	2.42	3.19	1.99	1.50	1.16
Parietal Secretion	4.69	5.84	9.36	4.46	3.54	3.58
NonParietal Secretion	8.01	8.66	8.24	9.44	10.66	14.92

Some very interesting information in this connection is obtained by estimating the activity of the acid-secreting cells by the method used by Gray, Bradley and Ivy.[5] This is based on the statement of Lui, Yuan and Lim,[6] and on that of Hollander,[7] that the secretion of the oxyntic cells contains approximately six milligrams of HCl. per cubic centimeter. Thus, by dividing the total milligrams of HCl. secreted by six, one obtains a figure representing the volume of "parietal secretion"; and by substracting this from the total volume, an index of the mucous and pyloric or diluting secretion. While these figures cannot be considered as more than estimated, they do provide a rough gauge of the activity of these cells.

These values, as they appear in Table II, suggest, also, that the activity of the acid-secreting cells in response to histamine is definitely diminished following the implantation of a pedicle jejunal graft, while that of the remaining cells is somewhat increased.

The p_H of the mucosa of the graft itself has been between 6.1 and 6.9, and, as noted above, the secretion of comparable areas of jejunum in isolated

loops was always at about that level (5.9 to 6.5), and contained no appreciable butter on titration.

Further evidence is also obtainable in the total chloride values which, while never increased after implantation of jejunal grafts, have on a number of occasions shown a marked decrease—proportional in some instances to the fall in acid secretion.

The burden of evidence suggests, therefore, that pedicle jejunal grafts implanted in the wall of the stomach also cause a quantitative reduction in the acidity and produce their effects chiefly by actual inhibition of the acid secretory mechanism—at least so far as its normal response to stimulatory effects of histamine or alcohol is concerned. Further than this, it would be unwise to go, based on experiments completed at present, but work now in progress is shedding additional light on the factors responsible and their mode of action.

Since it seems probable that gastric acidity, or something closely associated with it, is one of the important factors in the etiology and symptomatology of peptic ulcer, it occurs to one at once that such an operation as we are discussing should be tested in the laboratory both as to its influence in preventing the formation of ulcers produced under controlled experimental conditions and in the cure of such ulcers if, and when, produced.

Experiments of this sort were carried out, and the results have been reported.[8] It was found possible to produce duodenal erosions or ulcerations uniformly in nine control animals through the injection of a histamine-beeswax mixture (Figure 9) after the method of Varco and his associates,[9] whereas we were completely unable to bring about such changes in any of the three animals with pedicle jejunal grafts tested. The gastric analyses in such animals were also of interest, and the data from two animals with jejunal transplants and two controls are recorded in Table III. It will be seen that not only is the fasting free and total acidity markedly lower in the transplant animals than in the controls despite the prolonged exposure to histamine, but the normal response to the injection of one milligram of histamine is reversed. Such experiments present strong evidence of the efficacy of pedicle jejunal grafts in the wall of the stomach in preventing the formation of ulcers under strenuous experimental conditions and also in nullifying, in some way, the otherwise powerful effects of the prolonged administration of histamine on gastric acidity.

To test the curative effects of such grafts the histamine-beeswax mixture was administered to two animals until bloody stools were noted. They were then operated upon, and erosions in the duodenum similar to those seen in other animals observed through duodenotomy. This was then closed, and a pedicle jejunal graft implanted in the wall of the stomach. One animal died of bronchopneumonia 24 hours after operation, but, in the other, autopsy three weeks later showed the duodenum (Fig. 10) to be completely normal, despite the fact that the administration of the histamine-beeswax mixture in the same dosage had been continued throughout its life.

TABLE III

COMPARISON OF GASTRIC ANALYSES AFTER THE INJECTION OF 120 MG. OF HISTAMINE PHOSPHATE DAILY FOR 30 DAYS, IN ANIMALS WITH AND WITHOUT PEDICLE JEJUNAL GRAFTS

	Fasting	10 min after Histamine	20 min after Histamine
Dog #1704 (Graft)			
Free	50	40	0
Combined	38	32	25
Total	88	72	25
Dog #1777 (Graft)			
Free	30	28	18
Combined	30	24	22
Total	60	52	40
Dog #1710 (Control)			
Free	70	70	102
Combined	40	50	40
Total	110	120	142
Dog #1801 (Control)			
Free	70	74	90
Combined	38	40	30
Total	108	114	120

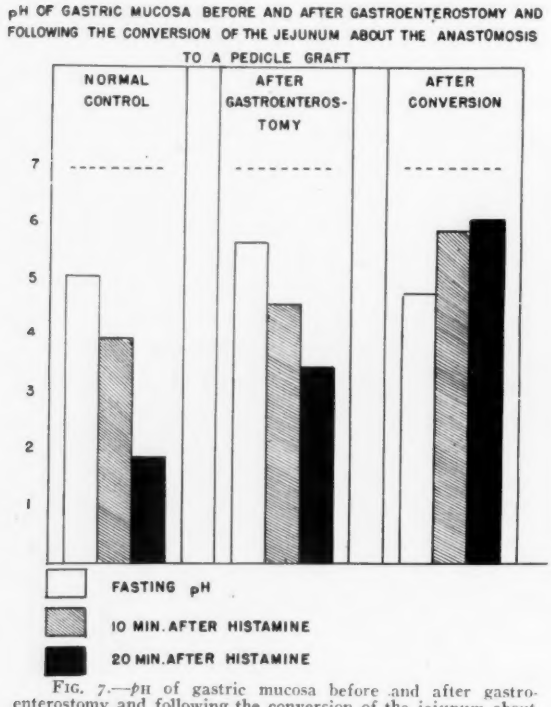

FIG. 7.—pH of gastric mucosa before and after gastroenterostomy and following the conversion of the jejunum about the anastomosis to a pedicle graft.

A sample of gastric juice obtained at the time of duodenotomy in this animal showed fasting free acidity of 80°, and a total of 130°. Ten days after the implantation of the jejunal graft, and despite the continued administration of histamine, the fasting free acidity was 34°, and the total 62°, both values falling still further after the additional injection of one milligram of histamine phosphate intramuscularly. Further evidence of the influence of such grafts in healing ulcerated areas is seen in our experience with

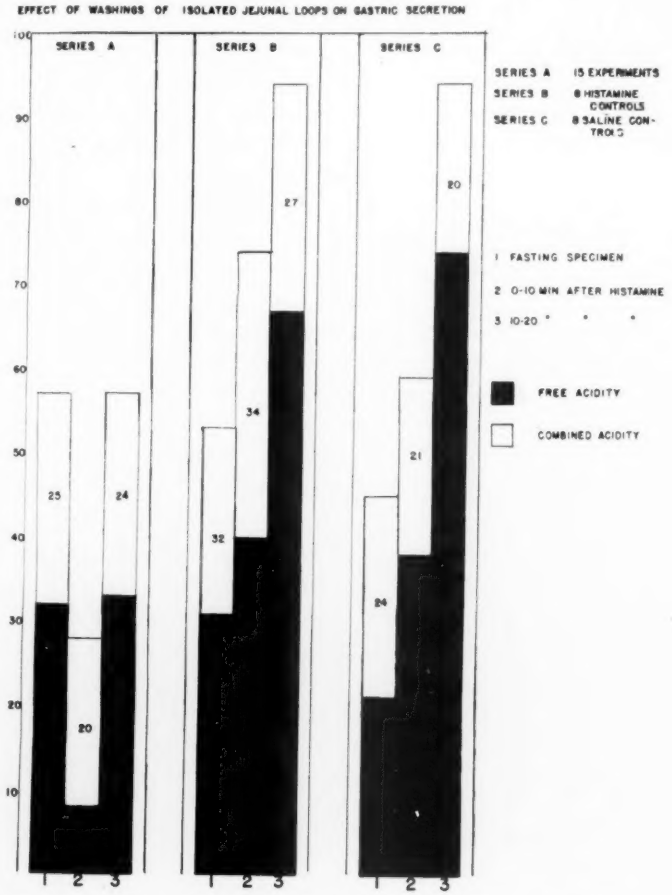

FIG. 8.—Effect of washings of isolated jejunal loops on gastric secretion.

Pavlov and Heidenhain-pouch animals. A number of these dogs developed ulceration about the external opening, which promptly healed when a graft was implanted in the wall of the pouch. However, despite the apparent correlation between the acid-inhibiting action of jejunal grafts and their preventive and curative effects in experimental ulcer in animals, we must be cautious in accepting this as the actual mode of action. As we know from follow-up studies in patients suffering from ulcer,[10] many patients are

completely cured, both symptomatically and objectively, despite acid values in the gastric analyses as high or higher than before operation.

Such results in animals naturally suggest the application of the method in the elective operative treatment of peptic ulcer in man, but before discussing the results of such an application we must mention certain other experimental findings pertinent to the selection of cases and to the evaluation of the method. First of all, it has been demonstrated repeatedly in animals that in the presence of a gastro-enterostomy or pyloroplasty the inhibitory effect of the pedicle jejunal graft is lost. The reasons for such an effect are not clear, but, obviously, until this can be further clarified it would exclude from consideration for operation all cases with organic pyloric obstruction. In addition, we have excluded cases of duodenal ulcer with any marked bleeding as unsuitable, at least until the efficacy of the method shall have been better established. We are left for the present, therefore, with two main indications: First, the group of uncomplicated ulcers which have resisted prolonged medical treatment; and, second, cases of marginal ulcer following gastro-enterostomy, without pyloric obstruction. It may be that further investigations will extend these indications, but it has seemed wise to limit the procedure to these groups, for the time being at least.

In the group of marginal ulcer following gastro-enterostomy, the operation is particularly useful, as it is much less of a procedure than the dismantling of a gastro-enterostomy followed by resection. In these cases the gastro-enterostomy is taken down, the edges of the gastric side of the anastomosis excised, and a pedicle jejunal graft implanted into the defect.

Soresi,[11] in 1915, reported the use of pedicle grafts of ileum in the plastic repair of pyloric stenosis due to ulcer in 18 cases, without a death, as well as in 11 instances of defects of the stomach and intestines, with only one leak. Although his proposals are purely from the point of view of plastic procedures and, as we now know, since the ileum was used, could not have had the effect noted with jejunal grafts, his report serves to indicate the possibility of survival of such a graft.

Our experience in animals indicates that if due care is taken to assure an adequate blood supply to the graft, it survives and is tolerated very well. This confirms the work of Dragstedt and Vaughn,[12] who implanted grafts from various levels of the intestinal tract, and from other organs, into the stomach to study their survival and the effect of the normal gastric secretion upon them, finding that all such grafts survived without evidence of pathologic alteration when their circulation was intact. This resistance to digestion by hydrochloric acid-pepsin mixture in the gastric juice in normal concentration is an attribute shared by many tissues when their nutrition is normal.

It may properly be asked, however, whether such grafts can survive, without injury, the effects of abnormal gastric secretion, such as is met with in the presence of peptic ulcer. The only evidence which we have bearing on this point is the fact that such a graft has survived when implanted

FIG. 9.—Photograph of experimental duodenal ulcer in a dog produced by the administration of 120 mg. of histamine phosphate daily.

into the stomach of an animal with a fasting free acidity of 80°, and a total acid of 130°, due to the prolonged administration of a histamine-beeswax mixture. In addition, roentgenologic studies of the patients operated upon show the grafts to be intact from three weeks to three months after implantation.

The risk would seem greatest during the first few weeks after the graft is implanted, and when the ulcer is still unhealed, as our studies in patients with ulcer indicate that a period of both quantitative and qualitative hypersecretion, at least so far as the hydrochloric acid is concerned, may occur temporarily after the operation as it has so far been carried out. Once this

FIG. 10.—Photograph of duodenum and pylorus in a dog in which duodenal erosions produced by histamine disappeared after the implantation of a pedicle jejunal graft.

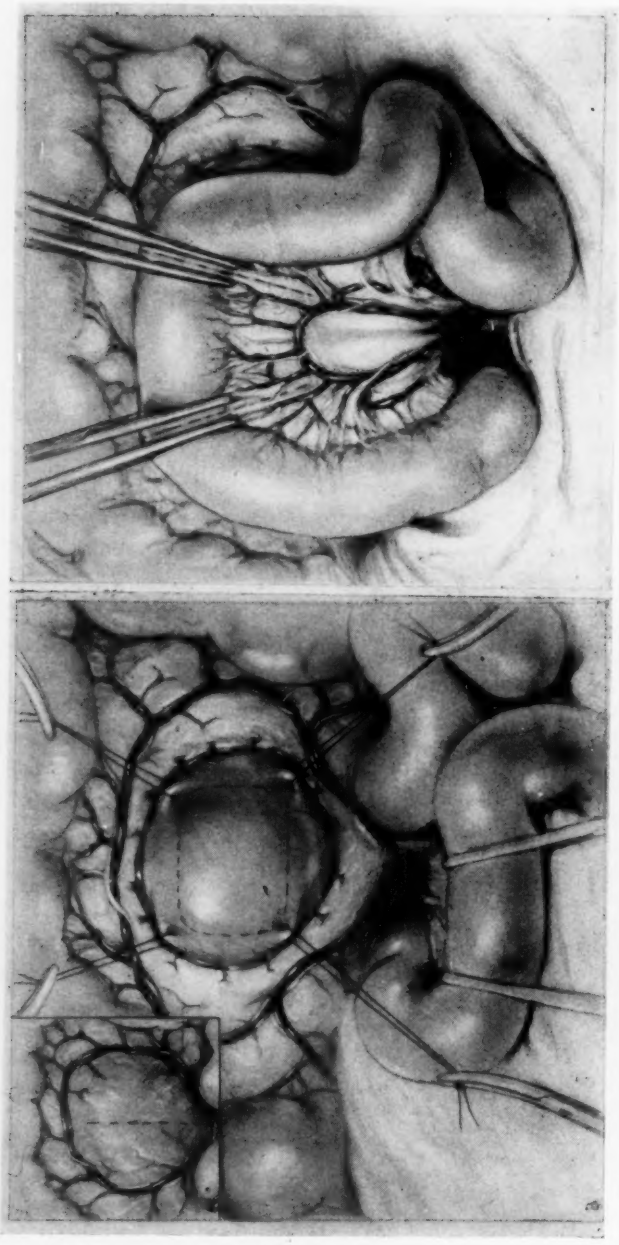

FIG. 12

FIG. 11

FIGS. 11-17.—Illustrating the steps in the operative procedures.

is past, however, the risk should be markedly reduced as the effect of the graft is to maintain the acid at a lower level and to modulate materially any tendency to rise as the result of various stimuli. This must be taken into consideration in evaluating the results of this operation in clinical cases of ulcer.

The operation as performed in clinical cases has been essentially the same as that in animals, with minor modifications. The steps in the procedure are as follows:

TECHNIC OF OPERATIVE PROCEDURES

(1) Either an upper left rectus or a transverse incision across the epigastrium gives adequate access to the operative site. After elevating the tranverse colon, a vertical incision is made just to the left of the middle colic artery, and extending from the base of the mesocolon upward as far as is safely possible. Through this opening the posterior wall of the stomach is delivered and the edge of the mesocolon sutured about an area some ten centimeters in diameter. Four traction sutures are placed in the wall of the stomach at the angles of the site in which the graft is to be implanted (Fig. 11).

(2) The selection of the donor site for the jejunal graft is, we believe, one of the most important steps in the entire operation, not because the property of influencing the gastric secretion appears to be confined to any narrow segment of jejunum, but because great care must be taken to select an area in which the distribution of vascular supply is such as to assure adequate circulation to the graft after transection of the bowel and the mesojejunum as far down as the arching branches of the superior mesenteric vessels. Since these latter course in the mesojejunum from two to five centimeters from the bowel, an incision between the shorter branches, as indicated in Figure 12, gives an adequate pedicle for the graft.

(3) When the appropriate site has been selected, usually about 25 to 30 cm. from Treitz' ligament, this segment of jejunum is isolated by dividing between pairs of Kocher clamps. The continuity of the intestine is restored by bringing together the proximal and distal clamps caudad to the graft and performing an end-to-end anastomosis, using mattress sutures of silk (Fig. 13).

(4) The Kocher clamps are now removed from the isolated segment, which is approximated at a point on its superior surface about one centimeter from the antemesenteric border to the lower, *i.e.*, lesser curvature, edge of the site previously selected in the posterior wall of the stomach, using a continuous suture of silk (Fig. 14).

(5) The isolated jejunal segment is now opened by excising approximately 1.5 cm. of its circumference at the antemesenteric border, and all bleeding points carefully ligated with No. 00 plain catgut (Fig. 14, inset).

(6) An area corresponding to the size of the opened segment of jejunum is now excised from the posterior wall of the stomach, one border being

FIG. 13

FIG. 14

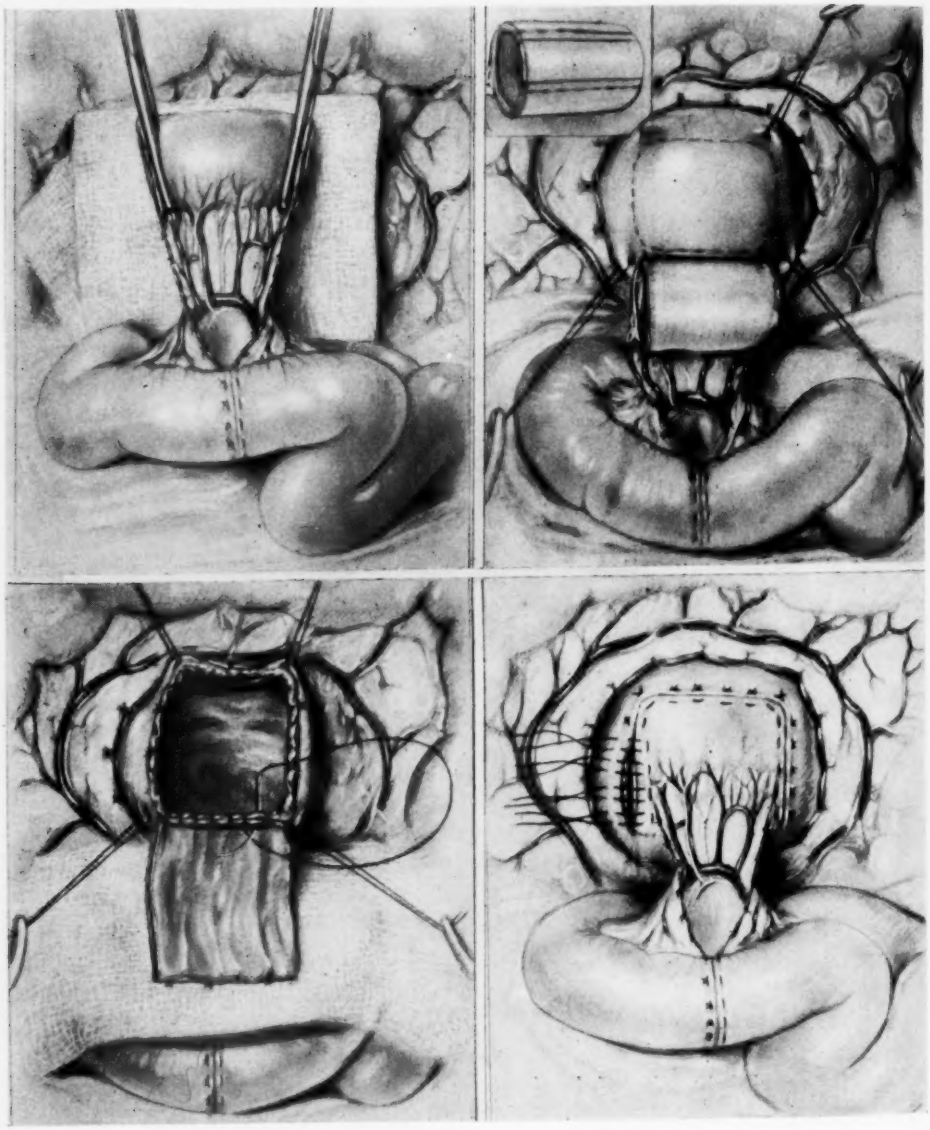

FIG. 15

FIG. 16

FIGS. 11-17.—Illustrating the steps in the operative procedure. (Cont.)

along the superior margin of the pedicle graft. A continuous lock-stitch of No. 1 chromic catgut is placed as reinforcement of the continuous silk suture (Fig. 15).

(7) The remaining edges of the graft are approximated to the borders of the defect in the gastric wall by means of mattress sutures of silk (Fig. 16).

(8) The bowel, just proximal and distal to the end-to-end anastomosis, is now tacked to the wall of the stomach at the site of the graft, and two serosal sutures of fine silk placed between the edges of the mesojejunal defect at the site of anastomosis and the edges of the mesenteric pedicle of the graft (Fig. 17). This is done to prevent the jejunum, when filled, from exerting traction at an angle on the pedicle of the graft.

CASE REPORTS

Case 1.—N. Y. H. History No. *270902*: V. G., a 20-year-old girl, was admitted to the New York Hospital because of recurrent epigastric pain of five years' duration. Two and one-half years previously an active duodenal ulcer was demonstrated roentgenographically. The symptoms at first responded to medical treatment but recurred, and, despite a careful dietary regimen, became much worse during the two months prior to admission. There had never been any vomiting nor any bleeding from the gastro-intestinal tract. Roentgenologic examination just before operation revealed the duodenal cap to be definitely defective with distinct crater formation. The secretory studies before operation are shown in Table IV.

TABLE IV

GASTRIC SECRETORY FINDINGS BEFORE AND AFTER IMPLANTATION OF PEDICLE GRAFT IN PATIENT V. G. (CASE 1)

	January 29, 1943								March 8, 1943							
Gastric Analysis	Fasting		0-10 min. after Hist.		10-20 min. after Hist.		20-30 min. after Hist.		Fasting		0-10 min. after Hist.		10-20 min. after Hist.		20-30 min. after Hist.	
	Vol.	11°F	Vol.	63°F	Vol.	90°F	Vol.	99°F	Vol.	11°F	Vol.	15°F	Vol.	12°F	Vol.	12°F
	40 cc	5°C 16°T	15 cc	5°C 68°T	20 cc	9°C 99°T	22 cc	14°C 115°T	36 cc	10°C 21°T	20 cc	10°C 25°T	16 cc	10°C 23°T	24 cc	10°C 22°T
mgm. HCl.	23.36		37.23		72.27		90.73		27.39		18.25		15.43		19.27	
mgm. HCl./cc.	.584		2.48		3.61		4.13		.77		.91		.84		.80	
Parietal Secretion	3.89		6.21		12.05		15.12		4.60		3.04		2.24		3.21	
NonParietal Secretion	36.11		8.79		7.95		6.88		31.40		16.96		13.76		20.79	
Total Cl. ME/L	85		117		109		136		94		89		88		73	
Neutral Cl.	69		49		10		23		75		64		65		51	
Total Cl. x Vol	3400		1755		2180		2992		3384		1780		1408		1752	

At operation, February 1, 1943, an ulcer was found in the duodenum, with a crater approximately one centimeter across. This was surrounded by an area of induration some four centimeters in diameter. A pedicle jejunal graft was implanted in the posterior wall of the stomach by the technic described above.

The postoperative course was entirely unremarkable, and all the ulcer symptoms

have been completely relieved. She was discharged from the hospital on the 19th postoperative day, and returned to her work as a typist six weeks after operation. Report of the roentgenograms taken on the 17th postoperative day states: "In contrast to previous examinations, in which the duodenal cap always appeared defective, the films on this occasion showed it to be entirely normal in size and shape. This certainly suggests marked improvement" (Fig. 18).

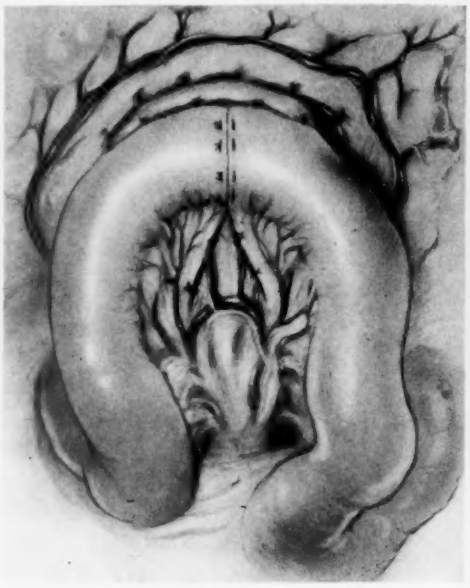

FIG. 17

FIGS. 11-17.—Illustrating the steps in the operative procedure. (Cont.)

The gastric analyses since operation have shown a gradual decline in free acidity after histamine—this value reaching 82° one week after operation, 66° on the 19th day, and 15° on the 35th day. The secretory findings five weeks after operation are shown in Table IV. During the intervening period, these figures trended steadily downward and have remained at or about the low level since that time. In this case, also, the evidences of diminished activity of the acid secretory mechanism is striking. These appear in the total chloride values before and after operation and in the total milligrams of hydrochloric acid secreted during 30 minutes after the administration of one milligram of histamine phosphate intramuscularly, which amounted to 200.23 mg. just before operation, and was only 51.95 mg. five weeks later. In the interval, this patient, like the others which we have been able to follow closely, had a considerable quantitative hypersecretion, although the gastric juice secreted contained less free and total acid.

The result in this patient has been excellent in the three and one-half months during which she has been observed. When seen on May 5, 1943, she had gained 15 pounds in weight, and her gastric analysis showed no free HCl. in the fasting specimen, with a rise to only 15° 30 minutes after histamine. The total HCl. secreted in the same period was only 19.69 mg.

Case 2.—N. Y. H. History No. 324713: V. Z., a 50-year-old, white, married, Lithuanian electrician, who had had symptoms of duodenal ulcer for three years. This pain had been accentuated with hunger, and, at first, was relieved by taking soda. His habits made dietary treatment of the ulcer impossible, as he indulged freely in both alcohol and tobacco, and he was, therefore, admitted to the hospital. Roentgenologic studies showed a defective duodenal cap and evidence of duodenitis (Fig. 19). Examination also revealed hypertensive cardiovascular disease, benign prostatic hypertrophy, and hepatomegaly. The gastric secretory findings before operation are shown in Table V. He was placed on a strict dietary regimen, with powders, but as his symptoms continued operation was decided upon.

At operation, March 1, 1943, a large ulcer was found located on the superior and posterior surface of the duodenum. The crater would easily admit the tip of the forefinger, and was surrounded by an area of marked induration. A pedicle jejunal graft was implanted by the usual technic.

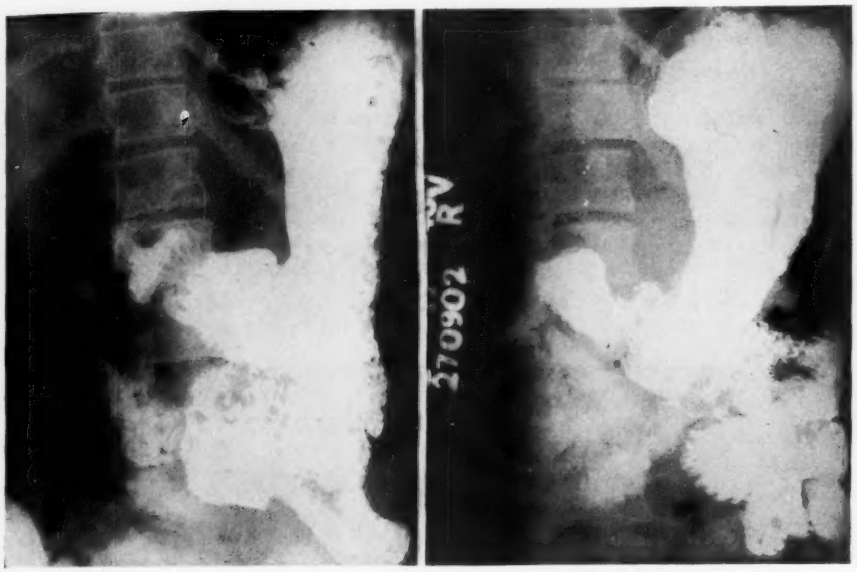

FIG. 18.—Case 1:—Pre- and postoperative roentgenograms of Patient V. G.

TABLE V

GASTRIC SECRETORY FINDINGS BEFORE AND AFTER IMPLANTATION OF PEDICLE GRAFT IN PATIENT V. Z. (CASE 2)

	March 9, 1943								May 3, 1943							
	Fasting		0-10 min. after Hist.		10-20 min. after Hist		20-30 min. after Hist.		Fasting		0-10 min. after Hist.		10-20 min. after Hist.		20-30 min. after Hist.	
Gastric Analysis	Vol.	0°F	Vol.	40°F	Vol.	75°F	Vol.	84°F	Vol.	20°F	Vol.	80°F	Vol.	117°F	Vol.	117°F
	55 cc	18°C 18°T	45 cc	19°C 59°T	35 cc	16°C 89°T	30 cc	11°C 95°T	87 cc	15°C 33°T	24 cc	11°C 91°T	23 cc	10°C 127°T	31 cc	11°C 128°T
mgm. HCl.	36.14		96.91		113.70		104.03		104.79		79.71		106.61		144.83	
mgm. HCl./cc.	.66		2.15		3.25		3.47		1.20		3.31		4.64		4.69	
Parietal Secretion	6.02		16.15		18.95		17.34		17.47		13.26		17.77		24.16	
NonParietal Secretion	48.98		28.85		16.05		12.66		69.53		10.74		5.23		6.84	
Total Cl.ME/L	85		122		140		145		86		136		155		155	
Neutral Cl.	65		63		51		50		53		45		28		27	
Total Cl.xVol.	4565		5490		4900		4350		7482		3264		3565		4805	

Following operation, he was completely relieved of his symptoms, and was discharged on the 17th postoperative day. Nine weeks after operation he had gained 25 pounds in weight, was still symptom-free, and was anxious to return to work. Although the gastric acidity fluctuated somewhat, there has been a definite reduction, and the findings on the latest analysis, nine weeks postoperative, are shown in Table V. Here, it will be seen that not only are the values for free and total acidity considerably reduced, but the same trend is reflected in the total chlorides of the gastric juice.

Case 3.—N. Y. H. History No. 318194: C. F., a 52-year-old, white, married American clerk, was first observed in the Out-Patient Department and complained of severe epigastric pain coming on two hours after meals, which was relieved by eating. These symptoms had been present intermittently for two years before he was admitted to the hospital for the first time in May, 1942. On that occasion, he was much relieved by diet, and was discharged after one week, and was referred to the Out-Patient Department. The symptoms recurred in January, 1943, and increased

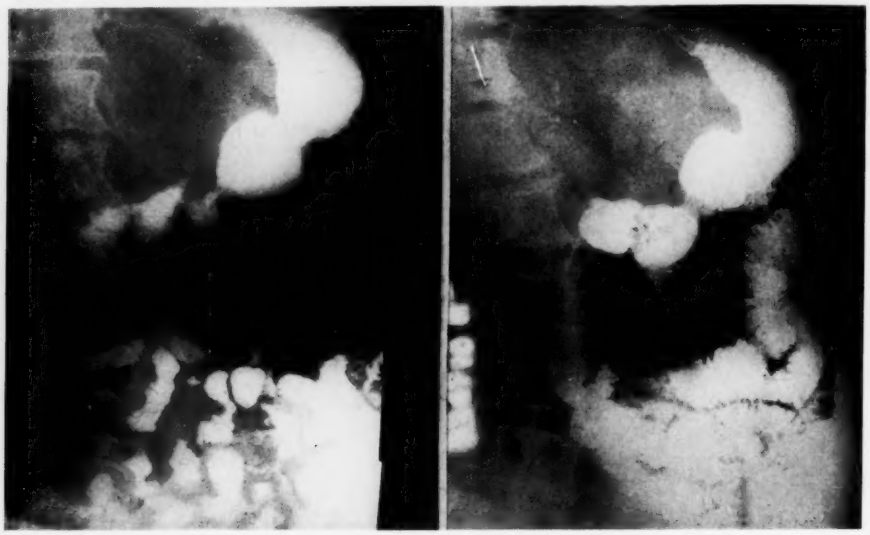

FIG. 19.—Case 2:—Pre- and postoperative roentgenograms of Patient V. Z.

in severity despite intensive medical treatment. On this occasion, there was considerable tenderness and some voluntary spasm in the epigastrium. Roentgenograms, March 15, 1943, revealed a large duodenal cap with a good-sized ulcer at the base. Physical examination revealed generalized arteriosclerosis, with hypertension. Gastric secretory findings before operation showed fasting free and total acidity values of 25° and 46°, respectively, rising to 79° and 96° within 30 minutes after histamine.

At operation, March 19, 1943, the upper abdomen was found to be the site of numerous fibrous adhesions in which the pylorus and first portion of the duodenum were buried. However, it was possible to palpate an ulcer on the posterior duodenal wall, with a definite crater. Considerable difficulty was experienced in elevating the transverse colon because of the adhesions, and the mesocolon was markedly shortened. The posterior aspect of the stomach was also the seat of many adhesions which had almost obliterated the lesser peritoneal sac. These were eventually severed, and the operation performed as outlined.

His postoperative course was entirely smooth, and he has been free of any symptoms referable to his ulcer. Incomplete gastric analysis, ten days after operation, showed

the free acid values to be considerably lower than before. Further studies have been impossible thus far, as the patient left town before these could be undertaken.

The result in this case has been good as far as symptoms are concerned, but until further information can be obtained, the effects of the procedure on gastric secretion must be considered as uncertain.

Case 4.—N. Y. H. History No. 324166: L. G., a 47-year-old colored woman had had epigastric distress after meals for nine years, which had been treated by diet and Sippy tablets. This pain was intermittent in character, and was accentuated on taking fried or fatty foods. Roentgenograms showed an active duodenal ulcer. The gastric secretory findings are shown in Table VI. The patient was placed on a modified Sippy regimen, with powders, and kept on strict bed rest. This failed to relieve her symptoms, however, and operation was decided upon.

TABLE VI

GASTRIC SECRETORY FINDINGS BEFORE AND AFTER IMPLANTATION OF PEDICLE GRAFT IN PATIENT L. G. (CASE 4)

	February 25, 1943								May 4, 1943							
	Fasting		0-10 min. after Hist.		10-20 min. after Hist.		20-30 min. after Hist.		Fasting		0-10 min. after Hist.		10-20 min. after Hist.		20-30 min. after Hist.	
Gastric Analysis	Vol.	0°F	Vol.	22°F	Vol.	39°F	Vol.	55°F	Vol.	29°F	Vol.	27°F	Vol.	30°F	Vol.	28°F
	25 cc	3°C 3°T	30 cc	23°C 45°T	25 cc	21°C 60°T	20 cc	27°C 82°T	142 cc	11°C 40°T	23 cc	10°C 37°T	6 cc	8°C 38°T	94 cc	11°C 39°T
mgm. HCl.	2.74		49.27		54.75		59.86		207.32		31.06		8.32		133.81	
mgm. HCl./cc.	.11		1.64		2.19		2.49		1.46		1.35		1.39		1.42	
Parietal Secretion	.46		8.21		9.13		9.98		34.55		5.17		1.39		22.30	
NonParietal Secretion	24.54		21.79		15.87		10.02		107.45		17.83		4.61		71.70	
Total Cl. ME/L	90		104		118		135		104		97		97		85	
Neutral Cl.	87		59		58		53		64		60		59		46	
Total Cl. x Vol	2250		3120		2950		2700		14768		2231		582		7990	

At operation, March 24, 1943, a pedicle jejunal graft was implanted. Since operation her symptoms have been entirely relieved, but up to May 3, 1943, 40 days after operation, she had continued to show very high values for free and total acidity. Similar findings have been observed for as long a period in other cases, which have later shown a diminished secretion. It must, therefore, be said that, as of 40 days after operation, the symptomatic result has been good, but that studies of the gastric secretion must be continued before the ultimate result can be appraised.

SUMMARY AND CONCLUSIONS

1. Experimental work is presented which indicates that a pedicle graft of jejunum when implanted into the wall of the stomach produces profound effects on gastric secretion.

2. These effects consist in a reduction of the fasting free acidity and a marked diminution, or actual reversal, of the normal response of the gastric acidity to such secretory stimulants as histamine and alcohol.

3. Such effects are not produced by the ordinary gastrojejunostomy but

appear promptly when the bowel about the stoma is converted to a pedicle graft and the normal continuity of the tract reestablished.

4. Grafts from the colon or ileum are without such action, while those taken from the duodenum are effective, but considerably less so than jejunal implants.

5. The presence of the factor responsible can be demonstrated in saline washings of isolated jejunal loops, and accumulated evidence indicates that its effects are exerted by actual inhibition of acid secretion, at least so far as the response to histamine is concerned, rather than by neutralization.

6. Pedicle jejunal grafts have been shown to be effective both in the prevention and in the cure of experimental ulcers produced in dogs by the prolonged administration of histamine phosphate.

7. It has been found that the effects of a pedicle jejunal graft are lost in the presence of a gastro-enterostomy or pyloroplasty.

8. The operation has been applied to patients with duodenal or marginal ulcer, with excellent immediate clinical results in all, and with gastric secretory changes in two of the three studied for a sufficient period after operation, which are similar to the alterations seen in the experimental animals. Since the third patient was the latest to be operated upon, it is entirely possible that similar changes may occur in her case.

9. It is suggested that if subsequent work confirms these findings, this may constitute a new approach to the problem of the surgical treatment of peptic ulcer.

10. This operation involves the transplantation of a portion of one organ of a physiologic system to a point elsewhere in that system, for the purpose of modifying the physiologic activity of the recipient organ. So far as we are aware, this utilizes a new principle in the field of surgery.

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Note: At the time of returning the proof of this paper the first four patients operated upon remain symptom free and have all resumed their occupations. In addition, the operation has been successfully performed in six other patients. The clinical and laboratory findings in this latter group will be reported at a later date.

DISCUSSION.—DR. LESTER R. DRAGSTEDT (Chicago): A new observation that throws fresh light on the pathogenesis or treatment of gastroduodenal ulcer is always welcome. Most of the experimental studies of the past few years are in harmony with the concept that the cause of ulcer is excessive continuous secretion of gastric juice both during digestion and, more importantly, during the interdigestive phase. The copious secretion at night, when the gastric glands are normally quiescent, is especially dangerous since the buffering effect of food is absent. The cause of this abnormal continuous secretion has not been determined, and it is here that the studies of Dr. Andrus, and his associates, seem to me to be very important. If it is due to the continuous formation in the body of histamine or some similar chemical substance, then we should expect, on the basis of this experimental work, that the transplantation of a jejunal patch into the stomach would be a successful method of treatment. On the other hand, if the continuous secretion is neurogenic in origin I should anticipate no beneficial effect. I am inclined to favor the latter view. In 1932, Mathews and I implanted segments of duodenum into the stomach of dogs. Valves were placed in the pylorus to prevent the backward regurgitation of the duodenal secretions. Under these conditions a typical perforating ulcer appeared in the duodenal transplant in one of the animals. This would seem to indicate that the duodenal mucosa has less resistance to gastric digestion than the stomach mucosa. While the situation in man may well be different from that obtaining in this experiment, nevertheless, it would seem prudent to watch these patients carefully for the possible formation of an ulcer in the jejunal transplant.

DR. J. SHELTON HORSLEY (Richmond, Va.): The work that was done by the authors is interesting. I would like to ask whether they found that the substance which inhibited the secretion of acid in the stomach decreased in its potency from the duodenum down to the ileum, and also whether it would be possible to prepare from the mucosa of the duodenum or jejunum an extract which might be efficient in the treatment of peptic ulcer.

Does the application of duodenal or jejunal mucosa to the stomach, as in pyloroplasty, or partial gastrectomy, or posterior gastro-enterostomy, simulate the transplantation of a graft from the jejunum to the stomach?

After the Billroth-I type of gastrectomy, when much of the stomach has been removed and the duodenum is flared open, it would seem that there would be ample contact between the duodenal mucosa and the stomach. In what respect does the grafting of a segment of the jejunum, with its blood supply intact, differ from gastric operations in which the mucosa of the duodenum or jejunum is united to the mucosa of the stomach?

DR. WILLIAM DEW. ANDRUS (closing): The experimental work which we have carried on to date, although still incomplete, suggests that the substance responsible for these effects does not act as a hormone, that it is not enterogastrone, and that it differs

from the substances contained in extracts of mucosa of the jejunum, with the possible exception of the "biodialysate," of Walawski. Some features of the jejunal grafts suggest that histaminase may be the responsible agent, but so far such histaminase as has been available to us has not been effective when placed in the lumen of the stomach. However, I do not feel that this can be excluded as yet.

Further work is in progress on the nature of the effects of such grafts, their mode of action and their effects when secretory stimuli other than histamine or alcohol are used.

GASTRIC HISTOLOGY AND SUBTOTAL GASTRECTOMY*

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THE PRESENT CONCEPTS of the gross and histologic features of "banal" gastritis are based almost completely upon data acquired from the study of resected specimens of the stomach. These became available with the adoption of partial gastrectomy as the operation of choice for gastric carcinoma and for many cases of gastric, duodenal, and jejunal peptic ulcer. The surgeon and pathologist previously hampered by the rapid postmortem changes which occurred in the gastric mucosa were now enabled, because of well preserved material, to accurately study the histologic nature of the changes in the mucosa of the stomach. Then, too, gastroscopy subsequently increased this growing interest, for it soon became necessary to correlate the gastroscopic findings with the actual histology of the gastric mucosa. Although isolated cases of simultaneous gastroscopic and histologic analyses could be found in texts and periodicals, no systematic study had been undertaken until recently, when several investigators studied the resected stomachs of patients who had been previously gastroscoped. A few observers studied microscopically the biopsies obtained through the gastroscope. Others, influenced by the findings in experimental animals attributed the gross and microscopic gastric mucosal changes to the ligation of the blood vessels and the action of acid upon such tissue deprived of its blood supply. Their conclusions, if true, would not only negate many of the accepted basic histologic concepts of gastritis, but would naturally exclude the resected stomach and duodenum as source materials.

This study was undertaken to determine whether any histologic alterations occurred in the stomach wall during the operation of subtotal gastrectomy. The group consisted of 35 ward patients upon whom this operation was performed. Duodenal ulcer was present in 25 patients, gastric ulcer in four, jejunal ulcer in three, peptic ulcer of the esophagus in one, and gastric carcinoma in two.

The preoperative treatment in all cases was essentially the same. The patients were deprived of food for 14 to 17 hours before operation. The stomach was gently aspirated and then lavaged with warm tap water by stomach tube four to six hours prior to operation. A Levine tube was then introduced, left *in situ,* and aspirated at intervals, so that a minimal amount of gastric secretion remained. Following anesthesia, the abdomen was opened and a biopsy was obtained from the anterior wall of the stomach approximately four centimeters proximal to the pylorus and two centimeters cephalad

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to the greater curvature. In the earlier cases a rubber covered intestinal clamp was applied across the biopsy site in order to avoid contamination of the peritoneal cavity when the specimen was excised. This precaution was soon found to be unnecessary, so that in the majority of cases the anterior wall of the stomach in this region was gently elevated with forceps and a segment was excised with a minimal amount of trauma. The resulting gastric defect was then closed by an inverting continuous linen suture. Following this the vascular supply of the portions of the stomach and duodenum which were to be resected were ligated. The De Petz clamp was then applied proximal to the reentrant angle, the stomach was divided and the duodenum transected.

TABLE I

No. of Cases	Interval between Original Biopsy and Removal of Resected Specimen
10	10–20 minutes.
9	20–29 minutes.
6	30–39 minutes.
3	40–49 minutes.
4	50–58 minutes.
3	Not recorded.

TABLE II

No. of Cases.	Interval between Removal of Resected Specimen and Fixation of Postresection Biopsy
30	1–5 minutes.
1	6 minutes.
2	10 minutes.
1	15 minutes.
1	35 minutes.

The interval between the original biopsy and the gastric resection varied from 10 to 58 minutes. (Table I) After the removal of the surgical specimen, additional pieces of gastric wall adjacent to the original biopsy were excised. (Table III) This site was chosen because gastritis produces only focal lesions in many cases, and any changes relative to the surgical procedure might be expected to be more intense around the previously traumatized biopsy site. The entire resected specimen was then opened, described, and fixed *in toto*, usually within 15 to 30 minutes after its removal. The earlier biopsies were fixed in Zenker-formol and formalin and the later ones in Bouin and formalin. In one case (Case 3) the gastric mucosa was exposed to the air for a period of 20 minutes while the specimen was being described. This produced alterations in the surface of the mucosa (Fig. 3b).

In describing the histologic findings of the original and post-resection biopsy specimens, the classification of gastritis presented by one of us[1] was employed.

A survey of the main features of each of these forms of gastritis is briefly presented:

1. Superficial Gastritis.—The stroma of the papilla is infiltrated by plasma cells, eosinophils, Russell bodies and lymphocytes in the chronic form, and

CLASSIFICATION OF GASTRITIS

1. Superficial—focal or diffuse:
   a. Acute—with or without erosions.
   b. Chronic—with or without erosions.
2. Interstitial—focal or diffuse:
   a. Acute.
   b. Chronic.
3. Atrophic:
   a. Productive and infiltrative—basal.
      1. Focal.
      2. Diffuse.
   b. Infiltrative—with or without follicle formation.
      1. Focal.
      2. Diffuse.
   c. Metaplastic.
      1. Focal.
      2. Diffuse.
   d. With focal hyperplasia of necks or pits and occasionally polyp formation.

by polymorphonuclear leukocytes in the acute type. Edema of variable degree is present in both acute and chronic superficial gastritis; erosions may occur in either.

2. Interstitial Gastritis.—The stroma between the necks of the gastric glands is infiltrated mainly by lymphocytes, which may form large aggregates or even follicles. In severe interstitial gastritis an increase in the collagenous fibers of the stroma occurs. Simultaneous atrophic changes in the neck portions of the glands result in distortion of the architecture of this region.

3. Atrophic Gastritis.—The greatest atrophic changes and alterations are encountered in this type of gastritis. The increase in collagenous tissue of the stroma and smooth muscle fibers derived from the muscularis mucosae, usually accompanied by cellular infiltration, are always associated with an atrophic disappearance of glandular elements, whether focal or diffuse. These changes can be so extensive that the entire mucosa with the exception of the surface cells may be replaced by infiltrated collagenomuscular tissue (productive and infiltrative type) or lymphoid aggregates or follicles (infiltrative type) or both. In the latter, the production of tumorous masses or even pyloric obstruction (pseudohypertrophy) may be observed.

In the metaplastic form the surface epithelium, or that of any portion of the gastric glands, may be replaced by intestinal, goblet, and even Paneth cells. These features are associated with changes of the infiltrative, or productive and infiltrative type. The involved areas of the mucosa significantly altered and functionally atrophic may show papular or diffuse thickenings (pseudohypertrophy).

The histologic findings in the original and postresection biopsies are summarized in Table III. Five cases are recorded in detail.

TABLE III

Path.* No.	Sex	Age in Years	Diagnosis**	Interval, in Minutes, between Incision in Abdomen and Original Biopsy	Interval, in Minutes, between Original Biopsy and Removal of Resected Specimen	Interval, in Minutes, between Removal of Resected Specimen and Postresection Biopsy	Site of Biopsies, Histologic Zone	Histologic Diagnosis Type of Gastritis***	
								Original Biopsy	Postresection Biopsy
68897*	M	30	Chronic peptic ulcer of duodenum	3	27	5	Antrum	Superficial — acute and chronic. Interstitial — acute and chronic. Atrophic—basal moderate chronic infiltrative and productive. Focal metaplastic.	Superficial—chronic. Interstitial—acute and chronic. Atrophic—basal moderate chronic infiltrative and productive.
70148*	M	23	Chronic peptic ulcer of duodenum.	5	18	2	Antrum	Superficial—chronic. Interstitial — acute and chronic. Atrophic — mild basal chronic infiltrative and productive.	Superficial—chronic. Interstitial — acute and chronic. Atrophic — mild basal chronic infiltrative and productive.
70257	M	30	Chronic peptic ulcer of duodenum**	10	55	2	T. Z. #	Superficial—mild chronic. Interstitial — focal subacute. Atrophic—basal chronic infiltrative and productive.	Superficial—chronic. Interstitial—chronic. Atrophic — basal chronic infiltrative and productive.
70258*	M	52	Jejunal ulcer	10	17	2	Corpus at T. Z.	*Corpus at T. Z.* Superficial—Chronic. Interstitial—chronic and focal acute. Atrophic—basal moderate chronic infiltrative and productive.	*Corpus at T. Z.* Superficial—chronic. Interstitial—chronic and focal acute. Atrophic — mild focal chronic basal infiltrative and productive.
							Antrum	*Antrum* Superficial—chronic. Interstitial—chronic with atrophy and mild acute. Atrophic—basal chronic infiltrative and productive.	*Antrum* Superficial—chronic. Interstitial — chronic with atrophy. Atrophic—basal chronic infiltrative and productive. Lymphoid follicles.
70308*	M	51	Chronic peptic ulcer of stomach.	30	10	5	Antrum	Superficial — chronic and focal acute. Interstitial—chronic and focal acute. Atrophic—basal chronic infiltrative and productive. Lymphoid follicles. Extensive metaplastic.	Superficial—chronic and focal acute. Interstitial—chronic and focal acute. Atrophic—basal chronic infiltrative and productive. Lymphoid follicles. Moderately extensive metaplastic.

TABLE III (Continued)

70343*	M	23	Chronic peptic ulcer of duodenum.	8	40	1	Antrum	Superficial—chronic. Interstitial—chronic and focal acute. Atrophic—basal subacute and chronic infiltrative and productive.	Superficial—chronic and focal acute with microscopic erosions.† Interstitial—chronic and focal acute. Atrophic—basal subacute and chronic infiltrative and productive. Lymphoid follicles. Small focus of acute.
70421*	F	56	Chronic peptic ulcer of duodenum**	N. R.##	25	5	Antrum	Superficial—chronic. Interstitial—chronic. Atrophic—basal chronic infiltrative and productive. Focal acute.	Superficial—chronic and focal acute. Interstitial—chronic and scattered focal acute. Atrophic—basal chronic infiltrative and productive. Lymphoid follicles. Focal acute.
70457*	M	54	Chronic peptic ulcer of duodenum.	2	35	10	Antrum	Superficial—chronic. Interstitial—chronic and acute. Atrophic—basal subacute and chronic infiltrative and productive. Lymphoid follicles.	Superficial—chronic. Interstitial—chronic and mild subacute. Atrophic—basal subacute and chronic infiltrative and productive. Lymphoid follicles and aggregates.
70584*	M	43	Peptic ulcer of duodenum in healed stage.	15	32	1	Corpus near T. Z.	Superficial—chronic. Interstitial—mild chronic and focal acute. Atrophic — basal mild chronic infiltrative and productive.	Superficial—chronic. Interstitial—mild chronic. Atrophic—basal mild and focal moderate chronic infiltrative and productive. Focal lymphoid aggregates.
70771*	M	28	Chronic peptic duodenal ulcer (at line of resection). Healing erosion of duodenum proximal to ulcer.	3	N. R.	5	Antrum	Superficial—chronic. Interstitial—chronic and acute. Atrophic—basal moderate chronic infiltrative and productive. Lymphoid aggregates and follicles. (Complete replacement of glands to necks in some foci.)	Superficial—chronic. Interstitial—chronic and focal acute. Atrophic—basal chronic infiltrative and productive. Lymphoid aggregates and follicles.
70971*	M	43	Ulcerated infiltrating scirrhous adenocarcinoma of stomach with lymph node involvement.	7	N. R.	4	Corpus near T. Z.	Superficial—mild chronic. Interstitial—mild chronic and focal acute. Atrophic — basal mild chronic infiltrative and productive. Focal wedges of severe involvement. Small lymphoid aggregates.	Superficial—mild chronic Interstitial—mild chronic and focal severe chronic. Focal acute. Atrophic—basal chronic infiltrative and productive. Focal wedges of severe involvement. Small lymphoid aggregates.
71341*	M	50	Healed peptic ulcer of duodenum.**	10	30	2	T. Z.	Superficial — mild and focal moderate chronic. Interstitial — mild and focal severe chronic. Atrophic — basal mild chronic infiltrative and productive, focally more severe.	Superficial—mild chronic. Interstitial — mild and focal severe chronic. Atrophic — basal focal moderate chronic infiltrative and productive.

TABLE III (Continued)

71476*	F	53	Healed ulceration of anterior wall of first portion of duodenum with stenosis.	5	23	2	T. Z.	*T. Z.* Superficial — moderate chronic. Interstitial — moderate chronic and acute. Atrophic—basal moderate chronic and subacute infiltrative and productive.	*T. Z.* Superficial — moderate chronic. Interstitial — mild to moderate chronic. Atrophic—basal moderate chronic infiltrative and productive.
							Antrum	*Antrum* Superficial—moderate to severe chronic. Interstitial — severe chronic and acute. Metaplastic necks. Atrophic—basal severe chronic infiltrative and productive. Lymphoid aggregates and follicles.	*Antrum* Superficial—moderate to severe chronic. Focal metaplasia of surface cells and pits. Interstitial — severe chronic and moderate acute. Metaplastic necks. Atrophic — basal severe chronic infiltrative and productive. Lymphoid aggregates and follicles. Focal metaplastic.
72820	M	61	Penetrating peptic gastric ulcer on lesser curvature.** Healed peptic ulcer of first portion of duodenum.**	10	40	2	Antrum	Superficial — moderate chronic. Interstitial—chronic and focal acute. Atrophic—basal chronic infiltrative and productive. Lymphoid aggregates.	Superficial—chronic. Interstitial—chronic and focal acute. Atrophic—basal chronic infiltrative and productive. Lymphoid aggregates and a few follicles.
73439	M	51	Scar of healed peptic ulcer of duodenum.**	5	25	2	Antrum	Superficial—chronic. Interstitial—chronic. Atrophic—basal moderate chronic infiltrative and productive. Lymphoid follicles.	Superficial—chronic. Interstitial—chronic and mild focal acute. Atrophic — basal mild chronic infiltrative and productive. Lymphoid follicles.
74109	M	41	Chronic penetrating and perforating peptic ulcer of duodenum.**	20	58	2	Antrum at T. Z.	Superficial—chronic. Interstitial—chronic with atrophic change. Atrophic—basal chronic infiltrative and some productive. Lymphoid aggregates and follicles.	Superficial—chronic. Interstitial—chronic with atrophic change. Atrophic—basal chronic infiltrative and productive. Lymphoid aggregates and follicles.
74421	M	49	Penetrating peptic ulcer of esophagus.**	5	30	2	Corpus near T. Z.	Superficial—chronic. Interstitial—focal chronic. Atrophic—basal chronic infiltrative and productive. Focal lymphoid follicles.	Superficial—chronic. Interstitial—focal chronic. Atrophic—basal mild focal chronic infiltrative and productive. Lymphoid aggregates and follicles.
74502	M	60	Chronic peptic ulcer of duodenum. Old gastroenterostomy.	10	30	2	T. Z. at antrum	Superficial—chronic. Interstitial—mild chronic with mild atrophy. Focal severe chronic. Atrophic—basal moderate chronic infiltrative and productive. Lymphoid aggregates.	Superficial—chronic. Interstitial — mild to moderate chronic. Atrophic—basal mild to moderate chronic infiltrative and productive. Focal metaplastic.

TABLE III (Continued)

74659	M	41	Scar tissue involving duodenum just beyond pylorus with resultant stenosis.**	6	24	35	T. Z. near antrum	Superficial—mild to moderate chronic. Interstitial—mild to moderate chronic with atrophy. Atrophic—basal moderate chronic infiltrative and productive. Focal acute inflammation of muscularis mucosae.	Superficial—mild to moderate chronic. Interstitial—mild to focal severe chronic. Atrophic—basal mild to moderate chronic infiltrative and productive. Lymphoid aggregates.
74795	F	52	Chronic peptic ulcer of duodenum. Pyloric stenosis.	15	45	1	Antrum	Superficial — moderate chronic. Interstitial—mild acute and moderately severe chronic. Atrophic—basal moderately severe chronic infiltrative and productive. Lymphoid aggregates and small follicles	Superficial — moderate chronic. Interstitial—mild acute and moderately severe chronic. Lymphoid follicles. Atrophic—basal moderately severe chronic infiltrative and productive. Lymphoid aggregates and small follicles.
75170	M	43	Scar of healed peptic ulcer of first portion of duodenum.**	3	16	2	Antrum	Superficial — moderate chronic. Interstitial — moderate chronic and mild acute. Atrophic—basal moderate chronic infiltrative and productive. Basal mild acute. Focal metaplastic. Lymphoid follicles.	Superficial — moderate chronic. Interstitial — moderate chronic and acute. Focal atrophy. Atrophic—basal moderate chronic infiltrative and productive. Basal mild acute. Focal metaplastic. Lymphoid follicles.
75213	M	47	Penetrating peptic ulcer of duodenum.**	2	23	5	T. Z.	Superficial—mild to moderate chronic. Interstitial—focal moderate chronic. Atrophic — basal focal mild chronic infiltrative and productive. Small lymphoid follicles.	Superficial—mild to moderate chronic. Interstitial—focal moderate chronic. Atrophic — basal focal mild chronic infiltrative and productive. Small lymphoid aggregates.
75330	M	46	Penetrating peptic ulcer of duodenum.	11	16	2	Antrum	Superficial — severe chronic. Interstitial — severe chronic. Atrophic — basal severe chronic infiltrative and productive. Large lymphoid follicles with focal complete replacement of mucosa.	Superficial — severe chronic. Interstitial — severe chronic. Atrophic — basal severe chronic infiltrative and productive. Extensive infiltration with lymphoid follicles and focal complete replacement of mucosa.
75642	M	49	Chronic peptic ulcer of duodenum.	7	N. R.	3	T. Z.	Superficial—mild to moderate chronic. Interstitial—focal mild and one focus of severe chronic. Atrophic — basal focal mild to severe chronic infiltrative and productive. Small lymphoid aggregate.	Superficial — mild chronic. Interstitial—mild focal chronic. Atrophic — basal focal mild to moderate chronic infiltrative and productive. Small lymphoid aggregate.

TABLE III (Continued)

75918	M	50	Puckered stellate scar of anterior wall of duodenum.**	14	25	15	T. Z.	Superficial—mild chronic. Interstitial — mild and focal moderate chronic. Atrophic — basal focal mild chronic infiltrative and productive. Focal lymphoid aggregate.	Superficial — mild to moderate chronic. Interstitial — mild to moderate chronic. Atrophic—basal mild to moderate chronic productive and infiltrative. Large lymphoid aggregate.
76542	M	40	Scars in anterior and posterior walls of first portion of duodenum.**	5	28	2	Corpus near T. Z.	Superficial—mild chronic. Interstitial — moderate and focal severe chronic with focal atrophic change. Atrophic—basal mild and focal moderate chronic infiltrative and productive. Lymphoid follicles.	Superficial—mild chronic Interstitial — moderate and focal severe chronic with focal atrophic change. Atrophic—basal mild and moderate chronic infiltrative and productive Lymphoid follicles.
76566	M	53	Chronic peptic ulcer of duodenum.	4	16	1	Corpus near T. Z.	Superficial — focal mild chronic. Interstitial — mild to moderate and focal severe chronic with atrophic change. Atrophic—basal mild to moderate and focal severe chronic infiltrative and productive. Lymphoid aggregates and follicles.	Superficial — focal mild chronic. Interstitial — mild to moderate and focal severe chronic with atrophic change. Atrophic—basal mild to moderate and focal severe chronic infiltrative and productive. Lymphoid aggregates and follicles.
76588	M	65	Scar in superior wall of 1st portion of duodenum.**	5	16	1	Antrum	Superficial—chronic. Interstitial—chronic with atrophic change and lymphoid follicles. Atrophic—basal moderate and focal severe chronic infiltrative and productive. Lymphoid aggregates and occasional follicle.	Superficial—chronic. Interstitial—chronic with atrophic change and lymphoid follicles. Atrophic—basal moderate and focal severe chronic infiltrative and productive. Lymphoid aggregates and occasional follicle.
76778	M	41	Healed peptic ulcer of anterior wall of 2nd portion of duodenum. Penetrating jejunal ulcer.**	5	50	3	Corpus near T. Z.	Superficial — moderate chronic. Interstitial—chronic and focal acute. Atrophic — basal mild chronic focal infiltrative and productive.	Superficial — moderate chronic. Interstitial—chronic and focal acute. Atrophic — basal mild chronic focal infiltrative and productive.
76831	M	57	Perforating peptic ulcer of pylorus.**	5	23	6	Antrum	Superficial—chronic. Interstitial—chronic with atrophic change. Focal metaplastic. Atrophic—basal moderately severe chronic infiltrative and productive. Lymphoid aggregates and follicles.	Superficial—chronic. Interstitial—chronic with atrophic change. Focal metaplastic. Atrophic—basal moderately severe chronic infiltrative and productive. Lymphoid aggregates and follicles.

TABLE III (Continued)

76865	M	53	Ulcerated infiltrating scirrhous adeno-carcinoma of stomach with involvement of lymph nodes.	2	31	2	Corpus at T. Z.	Superficial—none. Interstitial—none. Atrophic — basal focal chronic infiltrative and productive.	Superficial—none. Interstitial—small focus of moderate chronic. Atrophic — basal focal chronic infiltrative and productive.
76950	M	51	Chronic peptic ulcer of jejunum.	35	55	2	T. Z.	Superficial—mild to moderate chronic. Interstitial—focal moderate chronic. Atrophic—focal moderate basal chronic infiltrative and productive. Lymphoid aggregates. Focal extensive metaplastic with polymorphonuclear leukocytic infiltration and lymphoid aggregates and follicles.	Superficial—mild to moderate chronic. Interstitial—focal moderate chronic. Atrophic — moderate basal chronic infiltrative and productive. More lymphoid aggregates. Focal metaplastic.
77039	M	38	Several scars of anterior wall of pylorus.**	7	15	1	Antrum	Superficial — moderate chronic. Interstitial — severe chronic. Atrophic — severe basal chronic infiltrative with lymphoid follicles and moderate productive.	Superficial — moderate chronic. Interstitial — severe chronic. Atrophic — severe basal chronic infiltrative with lymphoid follicles and moderate productive.
77098	M	32	Scar of anterior duodenal wall with slight constriction of second portion of duodenum.**	5	12	2	T. Z.	Superficial—mild chronic. Interstitial—focal acute and chronic. Atrophic — mild basal chronic infiltrative and productive. Lymphoid aggregates.	Superficial—mild chronic. Interstitial—focal acute and chronic. Atrophic — mild basal chronic infiltrative and productive. Lymphoid aggregates.
77411	M	48	Peptic ulcer of anterior wall of duodenum. Scars of superior duodenal wall just beyond pylorus.** Duodenal erosion in healing state.	10	5	10	Antrum	Superficial—chronic. Interstitial—chronic with atrophy and focal acute. Atrophic — severe basal chronic infiltrative and productive. Lymphoid aggregates and follicles.	Superficial—chronic. Interstitial—chronic with atrophy and focal acute. Atrophic — severe basal chronic infiltrative and productive. Lymphoid aggregates and follicles.

Meaning of notations on table:

* Indicates the utilization of a rubber covered intestinal clamp to obtain the original biopsy.

** Designates the surgical diagnosis in those cases in which the ulcer was left *in situ*. All the others are pathologic diagnoses.

Case 1.—Path. No. 70308: Male, age 51, admitted in April, 1940. Three years before admission the patient had epigastric pain at irregular intervals after meals for a period of three months. A gastro-intestinal series, taken in 1937, demonstrated a moderately large ulcer involving the lesser curvature and posterior wall of the stomach. During the past four months there was increasingly severe epigastric pain and occasional vomiting. Roentgenograms demonstrated that the ulcer previously noted had diminished considerably in size. Wassermann—negative. Rehfuss' test meal—maximum free acid 30; maximum total acid 54. Night Rehfuss'—free acid 0; maximum total acid 32. Vagus test meal—maximum free acid 60; maximum total acid 82.

The patient was prepared with parenteral 5% glucose in physiologic saline. Prior to operation cevitamic acid, yeast tablets, vitamin B complex and nicotinic acid were administered by mouth, and seconal gr. 3 by rectum. Immediately before anesthesia, magendie minims 6 and atropine gr. 1/150 were given hypodermically.

Operation was performed, April 11, 1940, under cyclopropane anesthesia. The stomach was found to be slightly dilated. In the region of the coronary artery there was an indurated area which measured approximately four centimeters in diameter. This lesion presented a definite crater. The ulcer penetrated posteriorly and was sealed off by adherent jejunum which had found its way into the lesser sac.

The original biopsy was taken 30 minutes after incision of the abdomen, from the anterior wall of the stomach in the antral region two centimeters cephalad to the greater curvature. The resected specimen was removed ten minutes later. The post-resection biopsy was taken from the edges of the original biopsy wound five minutes after removal of the specimen. Both biopsies were cut into strips approximately one millimeter in width and fixed at once in Zenker-formol and formalin.

Histology of the Biopsies.—*Original Biopsy—Antrum.* (See Fig. 1a): The formalin-fixed tissue consists of four strips, two of which measure 1.5 cm. in length, a third which measures 1 cm. in length, and a fourth which measures 0.7 cm. in length. The Zenker-formol-fixed tissue consists of two pieces which measure 1.5 and 2 cm. in length, respectively.

The architecture of the mucosa is considerably altered. The surface, even on gross inspection, is irregularly nodular. The nodules are separated by depressed, widened, deeper pits. In a few areas, the glandular elements have been replaced by moderately cellular, very loose, edematous fibrous tissue infiltrated by plasma cells, a moderate number of eosinophils and a small number of polymorphonuclear leukocytes. Acini of neck and antral glands are scattered within this tissue. In the deeper third of the mucosa there is loose connective tissue of finely fibrillar character that contains numerous single muscle fibers and bundles of muscle fibers continuous with the muscularis mucosae and infiltrated by lymphocytes, plasma cells and a moderate number of eosinophils. Small lymphoid aggregates and lymphoid follicles surrounded by denser collagenous tissue and muscle bundles are present. In the neighborhood of some of these follicles there are antral glands of more regular appearance, with flattened basal nuclei. These portions of the mucosa occur between the depressed pits and are often wider than those occupied by the glandular elements.

The gastric glands are replaced by glands of intestinal type in large portions of each of the biopsy strips. These glands occupy only the superficial two-thirds or one-half of the mucosa. They are lined by columnar or cuboidal cells with neutrophilic

*** Diffuse unless specifically noted to be focal.

† The isolated observation of microscopi erosions in this case, in an exquisitely focal disease like gastritis, cannot be evaluated. No active erosions were found in any of the other 34 cases of this series.

‡ Transitional zone of the gastric mucosa between that of the corpus and that of the antrum. In this zone the peptic glands occupy a narrow portion of the mucosa just above the muscularis mucosae and antral glands, often containing acid cells, larger portions of the mucosa. In the antral region the antral glands extend to the muscularis mucosae.

‡‡ Interval not recorded.

or basophilic cytoplasm and brush borders. Goblet cells occur amongst them. Many of the nuclei are pseudostratified. They vary considerably in size, shape and staining intensity. A few of the nuclei are very large, with finely granular chromatin and large eosinophilic nucleoli. There are more mitoses among the intestinal cells than among the remnants of degenerating gastric glands. Around the intestinal glands there is loose moderately cellular fibrous tissue infiltrated by plasma cells, a moderate number of eosinophils and a few polymorphonuclear leukocytes.

FIG. 1a.—Path. No. 70308: Original biopsy (formalin fixed, magnification 62 times). Note complete replacement of gastric glands by those of intestinal type (atrophic metaplastic gastritis). Small group of antral glands in infiltrated musculocollagenous tissue (a). Small basal lymphoid aggregate (b). Atrophic basal productive and infiltrative gastritis. The width of the mucosa is unchanged.

Most of the mucosal surface is lined by cells which are of intestinal type. Pseudostratification, which produces the appearance of budding, is present in many areas. The nuclei are elevated to the free borders of the cells. Focally, the surface lining cells are markedly flattened, widened and distorted, with vacuolated cytoplasm and pyknotic nuclei. Polymorphonuclear leukocytes, an occasional eosinophile and some lymphocytes are present in or between these cells. In a few areas the surface lining cells contain atypical nuclei which are large, swollen, hyperchromatic, and bound by poorly outlined nuclear membranes. The basement membranes beneath the cells of intestinal type vary in their demarcation. Thin mucus, in which a few desquamated epithelial cells, a small number of polymorphonuclear leukocytes and some red blood cells are found, covers the surface of the mucosa.

The papillae vary in shape, many are edematous. Some are flat and wide, others are rounded and separated by the moderately wide lumina of glands lined by intestinal epithelium. In the Zenker-formal-fixed sections many contain fine, granular, eosinophilic material (fixed edema fluid). In a moderate number the eosinophilic material is very

dense and forms a homogenous layer between the capillaries and the basement membranes of the surface lining cells. The papillae are infiltrated by many plasma cells; some contain extravasated red blood cells.

In the portions of the mucosa replaced by collageno-muscular tissue, and deep to the intestinal glands, there are remnants of neck glands and antral acini. These are of degenerative character. In many of the cells no mucus is present along the free border. The nuclei are irregularly arranged and vary in size, shape and staining intensity. The basement membranes around the acini are barely visible or absent. Some

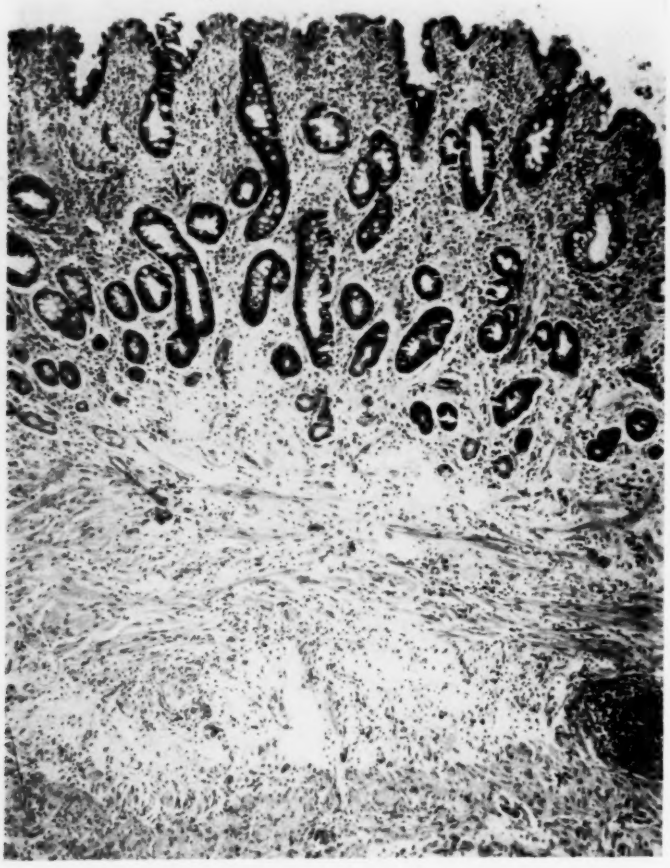


FIG. 1b.—Path. No. 70308: Post-resection biopsy (formalin fixed, magnification 62 times). The features are essentially similar to those described in Figure 1a. The surface cells in this area are slightly more distorted.

of the acini are dilated, and lined by narrow layers of cytoplasm. Scattered mitoses and a moderate number of argentaffine cells are present among these degenerating glandular acini. In the Zenker-formol-fixed section more gastric neck glands and antral glands are present. Russell bodies are found among the infiltrating cells in these regions. The junction of the muscularis mucosae with the mucosa is not clear in many places due to the proliferation of muscle fibers that extend into the upper half of the mucosa. Edema is evident throughout the mucosa but is most prominent in the papillae and just above the muscularis mucosae.

Capillaries are present within the superficial ⅓ to ¼ of the mucosa. These are of uneven caliber and measure from one to eight erythrocytes in diameter. The infiltrated musculo-collagenous tissue contains scattered venules of larger caliber which are so widely spaced that the mucosa appears relatively avascular. In the deeper portions of the mucosa there are capillaries filled with eosinophilic granular material and a few dilated lymphatic channels. The walls of the capillaries both here and in the papillae are not clear.

In the Zenker-formol-fixed sections the lymphoid aggregates and small follicles are more numerous than in those fixed in formalin. From these basal foci the muscularis

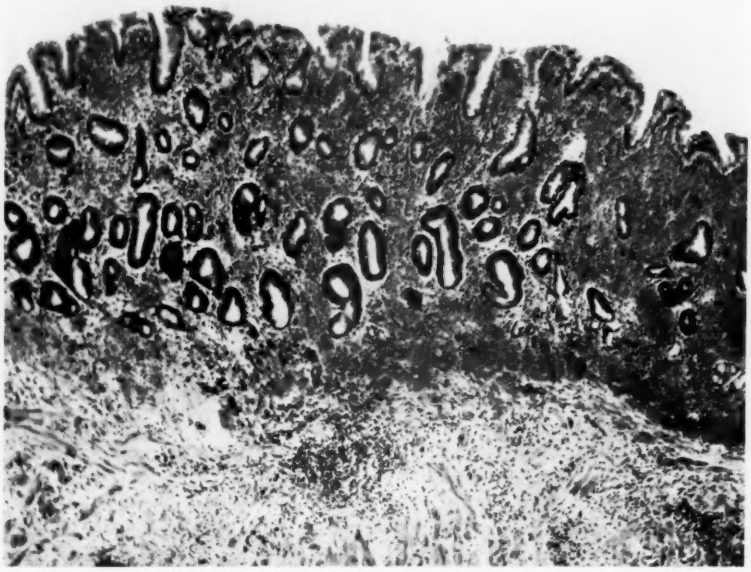


FIG. 1c.—Path. No. 70308: Post-resection biopsy (Zenker-formol fixed, magnification 62 times). Note the extensive mucosal hemorrhage. Character of the mucosa is otherwise similar to that of Figures 1a and 1b. Note the unchanged surface cells and glands.

mucosae is infiltrated by lymphocytes. In one place the lymphoid aggregates extend through the muscularis mucosae into the submucosa and focally replace the muscle fibers. The muscularis mucosae itself is edematous. The submucosa consists of loose connective tissue with dilated congested veins and arteries. Just beneath the muscularis mucosae there are some large dilated lymphatic channels. A few small islands of fat cells are present.

The septa of the muscularis propria contain extravasated red blood cells and foci of hemorrhage. The muscle cells are without significant change. The serosa contains congested capillaries and is slightly edematous.

Postresection Biopsy—Antrum (See Fig 1b): The formalin-fixed specimen consists of one strip, which measures 1 cm. in length. The Zenker-formol-fixed specimen consists of three strips, each of which measures 1 cm. in length.

The fundamental architecture of the mucosa is similar to that of the original biopsy. The surface is slightly less nodular. It is covered by mucus of slightly denser character that contains more polymorphonuclear leukocytes, some lymphocytes, and more erythrocytes.

The edema of the papillae, the congestion of the capillaries and venules in the superficial portions of the mucosa and the extravasation of erythrocytes are greater

than in the original biopsy sections. Above the muscularis mucosae the edema is slightly less intense.

One of the strips taken from the very edge of the original biopsy wound (see Fig. 1c) presents extensive hemorrhage into the mucosa. It is interesting to note that even here no greater changes are found in the surface lining cells than in the original biopsy specimens. The shape of the papillae is unaltered by the recent hemorrhage. The infiltrating cells are separated by the erythrocytes and appear less numerous, but the type of gastritis is similar.

Above the muscularis mucosae the congestion of the vessels is but slightly more prominent.

The submucosa is more edematous. Its vessels are more congested. Foci of extensive hemorrhage are present. Scattered through the submucosa are a few dilated lymphatic channels. The lumina of the dilated veins contain erythrocytes centrally, and polymorphonuclear leukocytes and some eosinophils along the endothelial lining of their walls. The septa of the muscularis propria and the serosa are without significant change.

Case 2.—Path. No. 72820: Male, age 61, was admitted to the hospital in November, 1940. He complained of aching intermittent epigastric pain of one and one-half years duration. The pain lasted for one to two hours, occurred irregularly, and subsided without treatment. During the past month the pain became more severe, lasted five to six hours, and was accompanied by anorexia and occasional vomiting. He had lost six pounds in weight and complained of increasing weakness. Wassermann—negative. Rehfuss' test meal—maximum free acid 65; maximum total acid 90. Night Rehfuss'—maximum free acid 34; maximum total acid 54. Vagus test meal—maximum free acid 60; maximum total acid 74.

The patient was prepared for operation with parenteral 5% glucose in physiologic saline. Magendie minims 6 and atropine gr. 1/150 were given hypodermically prior to anesthesia.

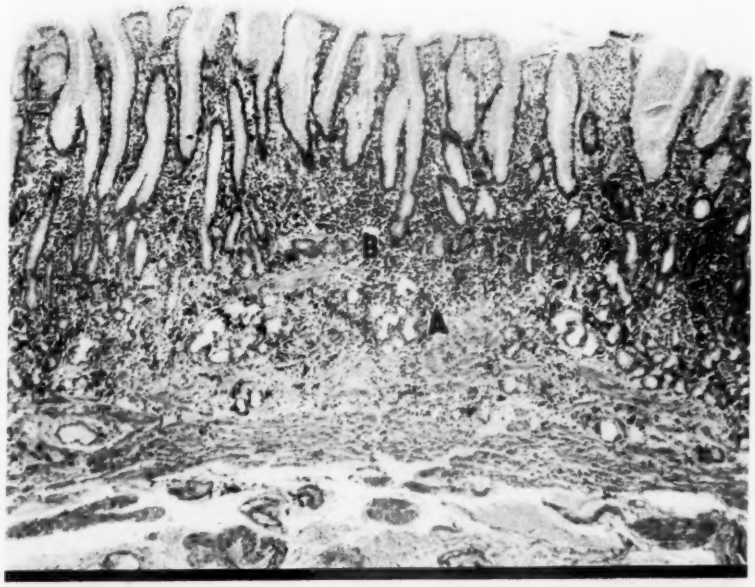
Operation was performed, November 14, 1940, under cyclopropane and ether anesthesia. The stomach was found to be slightly dilated. Scar tissue surrounded the first portion of the duodenum due to previous ulceration. Posteriorly, high on the lesser curvature near the esophagus, there was a penetrating ulcer whose base was formed by the pancreas. The lesion was surrounded by edema that extended to the reentrant angle. No enlarged lymph nodes were present. The ulcer was not removed, inasmuch as a Madelener procedure was performed.

The original biopsy was taken ten minutes after incision of the abdomen, from the anterior wall of the stomach in the antral region approximately two centimeters cephalad to the greater curvature. The resected specimen was removed 40 minutes later. Two minutes after its removal the post-resection biopsies were obtained from the edges of the original biopsy wound. Both biopsies were cut into narrow strips, approximately one millimeter in width, and placed in Bouin and formalin immediately.

Histology of the Biopsies.—*Original Biopsy—Antrum* (see Fig. 2a): The formalin specimen consists of two strips, each of which measures approximately 1.3 cm. in length; the Bouin specimen consists of two strips, each of which measures 1 cm. in length.

The architecture of the mucosa is moderately distorted in the neck region and more distorted in the basal portions of the mucosa occupied by the antral glands. These alterations are greater in the formalin-fixed specimens than in those fixed in Bouin. The surface of the mucosa in all the specimens is relatively flat except where the markings of the gastric areas are faintly discernible. Small, narrow linear fragments of mucus that contain a few polymorphonuclear leukocytes are scattered over the surface.

The surface lining cells over many of the papillae are relatively unchanged. Their nuclei are oval and occupy their usual position in the cell slightly above the base. Over some of the papillae, however, the surface cells show basal vacuolization and eleva-



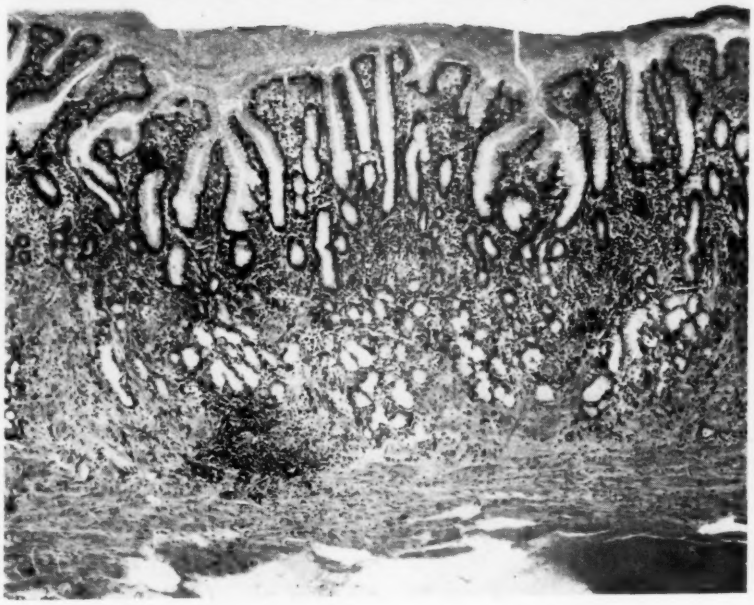


FIG. 2a.—Path. No. 72820: Original biopsy (Bouin fixed, magnification 62 times). Note the marked distortion of architecture and the bundles of muscle fibers. Islands of antral gland acini (A). Horizontal neck gland acini (B).

FIG. 2b.—Path. No. 72820: Post-resection biopsy (Bouin fixed, magnification 62 times). Note the edema of the papillae and the thick layer of mucus over the surface. The other features are essentially similar to those described in Figure 2a.

tion of the nuclei which are irregular in shape, position and staining intensity. The papillae contain a moderate number of plasma cells. Edema of the papillae varies so that some are wide and flat and others are pointed.

Some of the pits are slightly dilated and contain polymorphonuclear leukocytes; others are of average caliber. The neck glands are separated by stroma that is infiltrated with plasma cells, scattered eosinophils and some polymorphonuclear leukocytes. Around some of the necks small foci of polymorphonuclear leukocytes may be seen. Muscle bundles parallel to the surface of the mucosa penetrate to the pit-neck junctions, and form moderately large groups of fibers in some areas. The long axes of most of the neck glands are perpendicular to the surface of the mucosa; some are oblique. The basement membranes of many of the neck gland acini are no longer discernible. The lumina of some of the acini are dilated and contain polymorphonuclear leukocytes. The acini present a moderate number of mitoses and contain argentaffine cells. In some areas the neck gland acini are but shrunken remnants.

The antral glands in the basal half of the mucosa are decreased in number. They are replaced by bundles of smooth muscle fibers and by a smaller amount of collagenous tissue of finely fibrillar character. At some points continuity of the muscle bundles in the mucosa with the muscle fibers of the muscularis mucosae is evident. The fine fibrillar collagenous tissue is infiltrated by lymphocytes, occasional eosinophils and a few polymorphonuclear leukocytes. The groups of muscle fibers and the infiltrated collagenous tissue separate the antral glands from the muscularis mucosae and isolate small groups of antral acini. This produces the appearance of islands of acini in the altered stroma.

The antral gland acini are dilated, with many cells basally or superficially vacuolated. Their nuclei are irregular and vary considerably in character. These cellular changes occur in the islands of acini as well as in the closely approximated acini which lie in relatively unchanged stroma. In the latter areas, however, the nuclei are of more regular character. In the more dilated acini the lining cells are markedly flattened and contain but little or no mucus. Their nuclei are black, shrunken dots.

The portion of mucosa just above the muscularis mucosae contains lymphoid aggregates that extend into the muscularis mucosae at some points. In a few areas the lymphoid aggregates lie mainly within the muscularis mucosae. The muscle bundles of the latter are separated by edematous finely fibrillar tissue that is infiltrated by a moderate number of lymphocytes.

The capillaries of the papillae are congested and in places dilated. The walls of some of them are distinct; those of others merge with the basement membranes of the surface cells. The capillaries are of uneven caliber and are more dilated at the summits of the papillae than along the sides of the pits. These vessels range from one to two erythrocytes in width. There is a remarkable absence of visible vessels beneath the pit-neck junctions. Basally, above the muscularis mucosae dilated empty capillaries and venules are present.

The tissue of the submucosa is loose, somewhat edematous and contains moderately dilated, congested arteries and veins. Some of these vessels are filled with red blood cells and others with granular eosinophilic material. In the Bouin-fixed sections there are dilated lymphatic channels and small focal extravasations of erythrocytes.

The septa of the muscularis propria are slightly edematous. Around some of the nerves there is lymphocytic infiltration. An occasional eosinophile and lymphocyte is present around the venules of the septa. The serosa contains a few dilated congested venules and capillaries.

Postresection Biopsy—Antrum (see Fig. 2b): The formalin-fixed specimen consists of two pieces which measure 1.5 and 1.6 cm., respectively. The Bouin-fixed specimen consists of two pieces which measure 0.9 and 1 cm., respectively.

The microscopic architecture of the mucosa and its surface markings correspond to

those of the original biopsy. The surface of the mucosa is covered by a wider layer of denser mucus that contains numerous erythrocytes and small clumps of polymorphonuclear leukocytes. The entire mucosa is more edematous than that of the original biopsy. The edema is better seen in the Bouin-fixed, than in the formalin-fixed tissue. More of the surface cells show basal vacuolization than those of the original biopsy. However, even over areas of marked edema of the papillae, the vacuolization of the individual cells is not greater. The other changes of the surface cells, of the neck glands, and of the antral glands described in the original biopsy are seen here. The infiltrating cells are similar in their distribution and number.

The capillaries of the papillae are more congested but of somewhat narrower caliber. Most of them are but one erythrocyte in width. The changes in their walls are similar to those already noted in the original biopsy. Above the muscularis mucosae the degree of vascular congestion is similar to that of the original biopsy except for an occasional dilated congested vein that penetrates the muscularis mucosae from the submucosa.

The most marked differences in the gastric wall are seen in the submucosa. There is extensive edema and hemorrhage near the edges of the original biopsy wound. The arteries and veins are considerably dilated and congested. The walls of the veins are infiltrated by polymorphonuclear leukocytes. At a distance from the edges of the original biopsy the hemorrhage is focal and the edema is less prominent, but the congestion and dilatation of the vessels is similar. Erythrocytes extend into the septa of the muscularis propria from the areas of extensive hemorrhage in the submucosa. The capillaries of the muscularis propria, especially those near the serosa, are congested and surrounded by small foci of hemorrhage. Many of the capillaries and small venules are filled with polymorphonuclear leukocytes that infiltrate their walls and extend into the adjacent fibrous tissue and muscle fibers. The serosa is similar to that of the original biopsy sections.

Case 3.—Path. No. 74659: Male, age 41, entered the hospital in April, 1941. The patient was well until three years ago when he had one unheralded hematemesis. Since then he experienced epigastric pains and belching. For the past four months he complained of right upper quadrant pain and vomiting. Two months ago he had had melena. Two days prior to admission he suffered severe cramp-like pains accompanied by vomiting. Wassermann—negative. Rehfuss' test meal—maximum free acid 50; maximum total acid 70. Night Rehfuss'—maximum free acid 44; maximum total acid 52.

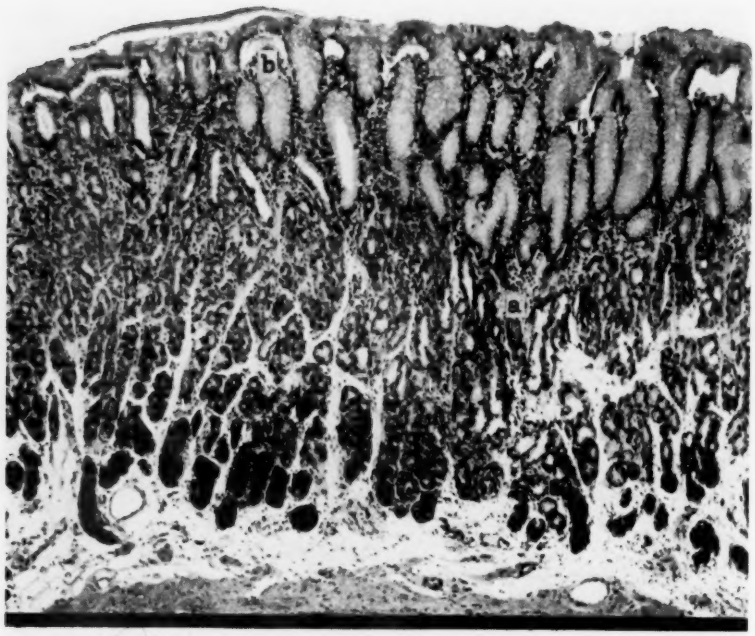
The patient was prepared for operation with parenteral 5% glucose in physiologic saline. Immediately before anesthesia, magendie minims 6 and atropine gr. 1/150 were given hypodermically.

Operation.—April 21, 1941: Under spinal anesthesia, with 12 cc. of Jones solution supplemented with ethylene and ether. The stomach was dilated to two and one-half times its usual size. There was increased vascularity. Scar tissue which surrounded the duodenum immediately beyond the pylorus narrowed it to a diameter of one-half inch.

The original biopsy specimen was taken six minutes after incision of the abdomen from the anterior wall of the stomach in the transitional zone near the antrum approximately two centimeters cephalad to the greater curvature of the stomach. The resected specimen was removed 24 minutes later. The original biopsy specimens were cut into strips approximately 1 mm. in width and fixed in formalin and Bouin at once. The entire specimen was then described with minimal manipulation. Thirty-five minutes after its removal it was fixed in toto in Bouin solution. Sections of the edges of the original biopsy wound were then taken from the fixed specimen.

Histology of the Biopsies.—*Original Biopsy—Transitional Zone* (see Fig. 3a): The formalin-fixed specimen consists of three strips that measure 0.5, 0.7 and 0.8 cm., respectively. The Bouin specimen consists of two strips which measure 1.0 and 1.2 cm.

The mucosal architecture is generally unchanged. There is focal distortion in the



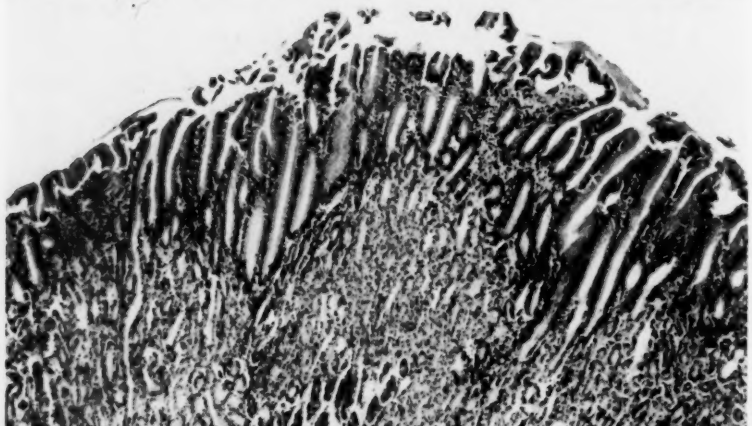


FIG. 3a.—Path. No. 74659: Original biopsy (Bouin fixed, magnification 62 times). Note the separation of the surface cells from the papillae (artefact). The latter vary in width, height, and degree of infiltration. Focal mild interstitial gastritis (a). The glands are elevated from the muscularis mucosae and separated from each other by edematous, infiltrated, finely fibrillar, connective tissue. Suprapapillary space filled with edema fluid (b).

FIG. 3b.—Path. No. 74659: Post-resection biopsy (Bouin fixed, magnification 52 times). Note the elongation of pits and necks, widening of the pits and focal villiform papillae produced by prolonged exposure to air before fixation. Basal edema is slightly greater than in the original biopsy. The summits of some of the papillae are torn (artefact). The other features are similar to those seen in Figure 3a.

neck region and above the muscularis mucosae. The surface of the mucosa is flat. The gastric areas are not discernible. A thin layer of mucus that contains a few desquamated epithelial cells, an occasional polymorphonuclear leukocyte and erythrocytes covers portions of the mucosal surface and fills the pits.

The formalin-fixed tissue differs from that fixed in Bouin. In the former the majority of the surface cells contain the usual amount of mucus. Most of their nuclei are oval or round; some are concave superficially and irregular. The surface cells over a few of the papillae contain no mucus and are shorter than the cells adjacent to them. Their cytoplasm is basophilic. Some of the nuclei occupy almost the entire cell, whereas others are at the free border. Focal pseudostratification is present in these areas. A moderate number of the cells, over both infiltrated and noninfiltrated papillae, are vacuolated basally. In the Bouin-fixed sections most of the surface cells are separated from the summits of the papillae by spaces. The major number of these spaces are empty; some contain eosinophilic granular material. The basal portions of many of the cells are no longer lined by basement membranes and are not clear. The nuclei, however, are not changed. In a few places the thin basement membranes are still visible beneath the cells. Here the basal changes in the cells are similar to those described in the formalin-fixed tissue.

The papillae vary in shape. Some are pointed; others are flat. Many are infiltrated by a moderate number of plasma cells, some lymphocytes and an occasional eosinophile or polymorphonuclear leukocyte. In these papillae there are more stromal nuclei. A small number of papillae contain extravasated red blood cells; others contain large amounts of eosinophilic, smooth material (fixed edema fluid). A few contain only edema fluid. In the Bouin-fixed sections the edema of the papillae is not as evident due to the expression of the serum into the spaces already noted between the surface cells and the summits of the papillae. The degree of infiltration is similar to that described in the formalin-fixed sections. The summits of the papillae beneath the spaces are covered by thickened, collagenous membranes of neutrophilic character.

The pits occupy one-fifth to one-quarter of the entire thickness of the mucosa. The neck glands are separated by edematous connective tissue infiltrated by small numbers of plasma cells, some lymphocytes and a few eosinophils. Their acini are surrounded by basement membranes. In a few areas no recognizable basement membranes are present. The neck cells of these acini are basally vacuolated; the acid cells are vacuolated, shrunken or deeply eosinophilic. There are small foci of denser lymphocytic infiltration between some of the neck acini. Amongst the lymphocytes a single degenerating deformed acinus is present, lined by irregular cells. In one such area the neck cells of the acinus are basophilic and granular. The cytoplasm approaches that of intestinal epithelium (dedifferentiation).

The glands in the middle third of the mucosa are separated by edematous, finely fibrillar, connective tissue that contains a small number of plasma cells and lymphocytes. There is one small aggregate of lymphocytes between the glands at this level of the mucosa. The peptic glands in the basal portions of the mucosa are separated from the muscularis mucosae by edematous finely fibrillar, infiltrated, connective tissue. At some points the peptic gland acini reach the muscularis mucosae. The glands nearest the muscularis mucosae contain peptic cells whose nuclei are near or at their free borders. The acid cells in these acini contain three to five nuclei, some of which are faintly stained and shrunken. The basement membranes of these acini may be thickened or absent. The cells of the latter merge with the edematous fibrillar connective tissue.

The mucosal glands in the formalin-fixed tissue are more closely approximated than in the Bouin-fixed specimens. This is due to less evident edema of the mucosa in the former sections.

The capillaries of the papillae in the Bouin-fixed sections are empty. They vary from one to three erythrocytes in width. At the pit-neck junctions there are venules

which vary from six to eight erythrocytes in width. Their walls are thickened. In the lower two-thirds of the mucosa there are scattered empty venules eight erythrocytes in width. Immediately above the muscularis mucosae there are dilated venules that contain eosinophilic granular material and erythrocytes. In the formalin-fixed sections the distribution of the vessels is more evident. Extravasation of red blood cells in the papillae and in small foci in the neck region are also more evident in these sections.

The demarcation of the mucosa from the muscularis mucosae is clear. The latter is edematous and contains a few lymphocytes and dilated venules which are empty or contain eosinophilic granular material. The arterioles within it are contracted. The submucosa in the Bouin-fixed tissue is edematous. The veins are dilated and contain eosinophilic granular material and some erythrocytes. The arterioles are contracted; the arteries are dilated and congested.

The septa of the muscularis propria are edematous and contain a small number of lymphocytes in some places. The serosa is moderately edematous.

Postresection Biopsy—Transitional Zone (see Fig. 3b): The specimen consists only of Bouin-fixed tissue from the edges of the biopsy wound. One strip is 1.5 cm. and the other 2.5 cm. in length.

The mucosal architecture is essentially similar to that of the original biopsy. In some areas the pits are longer and the papillae elongated and narrower. Most of the pits are empty. The surface is flat. The gastric areas are not discernible. A thick layer of denser mucus that contains desquamated epithelial cells and masses of erythrocytes covers the surface. Among the erythrocytes there are strands of fibrin and in places many polymorphonuclear leukocytes. The amount of mucus in the surface cells over some of the papillae is less than in the original biopsy. Generally, however, the amount of intracellular mucus is similar.

The cellular infiltration of the papillae and of the stroma between the neck glands is focally greater than in the original biopsy. The edema of the upper two-thirds of the mucosa is less. Basally, however, in some areas the edema is greater. The pits, neck gland acini and peptic gland acini are essentially similar. The deepest of the peptic gland acini are often completely surrounded by edematous, finely fibrillar, infiltrated, connective tissue.

The vascular distribution within the mucosa does not differ. Some of the venules near the muscularis mucosae contain polymorphonuclear leukocytes in their lumina and walls. These cells extend for a short distance into the surrounding tissue.

The muscularis mucosae is thinner. The infiltration within it and the edema are similar. The upper layers of the submucosa beneath the muscularis mucosae are occupied by large foci of hemorrhage. The veins and arteries are more dilated. They are congested and contain polymorphonuclear leukocytes which extend into the walls of some of the veins.

The septa of the muscularis propria adjacent to the submucosa are edematous. Some of the capillaries and venules within the septa contain polymorphonuclear leukocytes that extend into the walls of the vessels. Near the serosa the edema is less than in the original biopsy specimens. The serosa is less edematous.

Case 4.—Path. No. 75213: Male, age 47, was admitted to the hospital in May, 1941. He complained of sticking postprandial epigastric pain penetrating to the back, and occasional tarry stools for the past ten months. A gastro-intestinal series demonstrated a duodenal ulcer. This responded to medical therapy until two months ago when the pain became intractable. Wassermann negative. Rehfuss' test meal—maximum free acid 40; maximum total acid 60.

The patient was prepared for operation with parenteral 5% glucose in physiologic saline. Magendie minims 6 and atropine gr. 1/150 were given hypodermically before anesthesia.

Operation.—June 5, 1941: Under spinal anesthesia, with 12 cc. of Jones solution supplemented by intravenous sodium pentothal. The stomach was found to be of normal size. Distal to the pylorus there was a mass of indurated tissue that pushed the duodenum to the left. A penetrating ulcer sealed by omentum occupied the superior portion of the duodenum. A resection with post-pyloric "auschaltung" was performed.

The original biopsy was taken two minutes after incision of the abdomen, from the anterior wall of the stomach in the transitional zone near the antrum, approximately two centimeters cephalad to the greater curvature. The resected specimen was removed 23 minutes later. Sections were taken from the edges of the original biopsy wound five minutes after removal of the stomach. Both biopsies were cut into strips, approximately one millimeter in width, and placed in Bouin and formalin immediately.

Histology of the Biopsies.—*Original Biopsy—Transitional Zone* (see Fig. 4a): The formalin specimen consists of three strips which measure 0.8, 0.7, and 1 cm., respectively. The Bouin specimen consists of three strips which measure 1.1, 1.2 and 1.5 cm., respectively.

The architecture of the mucosa is unchanged except basally above the muscularis mucosae. The junction between the muscularic mucosae and the mucosa is clear. The mucosal surface is slightly wavy, and, focally, presents gastric area markings. The surface is covered by narrow strands of mucus that contain a rare desquamated epithelial cell.

The surface cells contain an average amount of mucus. Their nuclei vary in shape, size, staining intensity and position. The long axes of many of the nuclei are parallel to the free surfaces of the cells. Focal pseudostratification of the nuclei is present. The basal portions of many of the surface cells contain moderately extensive vacuoles. A rare cell is vacuolated superficially. The vacuolization is not related to the amount of edema or infiltration of the papillae or the degree of congestion of their capillaries.

The papillae vary in character. Some are narrow and uninfiltrated; others are wide. The latter contain a greater number of stromal cells than is usually seen—small numbers of plasma cells and lymphocytes, and scattered Russell bodies. Many of the papillae contain eosinophilic granular material (edema); a few contain a small number of extravasated red blood cells.

The majority of the neck glands are closely approximated and separated by their basement membranes and by the small amount of stroma usually present in this region. Focally, there is lymphocytic infiltration around acini of degenerative character, and increase in the number of stromal cells. The lining cells of the acini are vacuolated; their nuclei vary in size and position. Some of the acini of the neck glands are lined by cells with eosinophilic cytoplasm and pyknotic nuclei; others near the pit-junctions are dilated and lined by flattened eosinophilic neck cells and acid cells. Their lumina contain granular eosinophilic material.

Most of the peptic glands in the basal portions of the mucosa are closely approximated. There is the usual small amount of stroma between them. Those just above the muscularis mucosae are surrounded by thickened basement membranes which are focally widened, smooth and eosinophilic. The nuclei of the peptic cells of these acini vary in size and shape and in their position within the cell. Some of the nuclei are near or at the free borders of the cell despite the fasting state of the mucosa. Such dispolarity of the nuclei occurs less frequently in the superficial portions of the mucosa. A few of the acid cells of these acini contain two or three nuclei. The glandular acini in scattered areas are separated from the muscularis mucosae by finely fibrillar collagenous tissue infiltrated with lymphocytes, a small number of eosinophils and a few polymorphonuclear leukocytes. The stromal nuclei in these foci are increased. Single peptic gland acini with shrunken and degenerating acid and peptic cells are enclosed within this tissue, and merge indefinitely with it. There

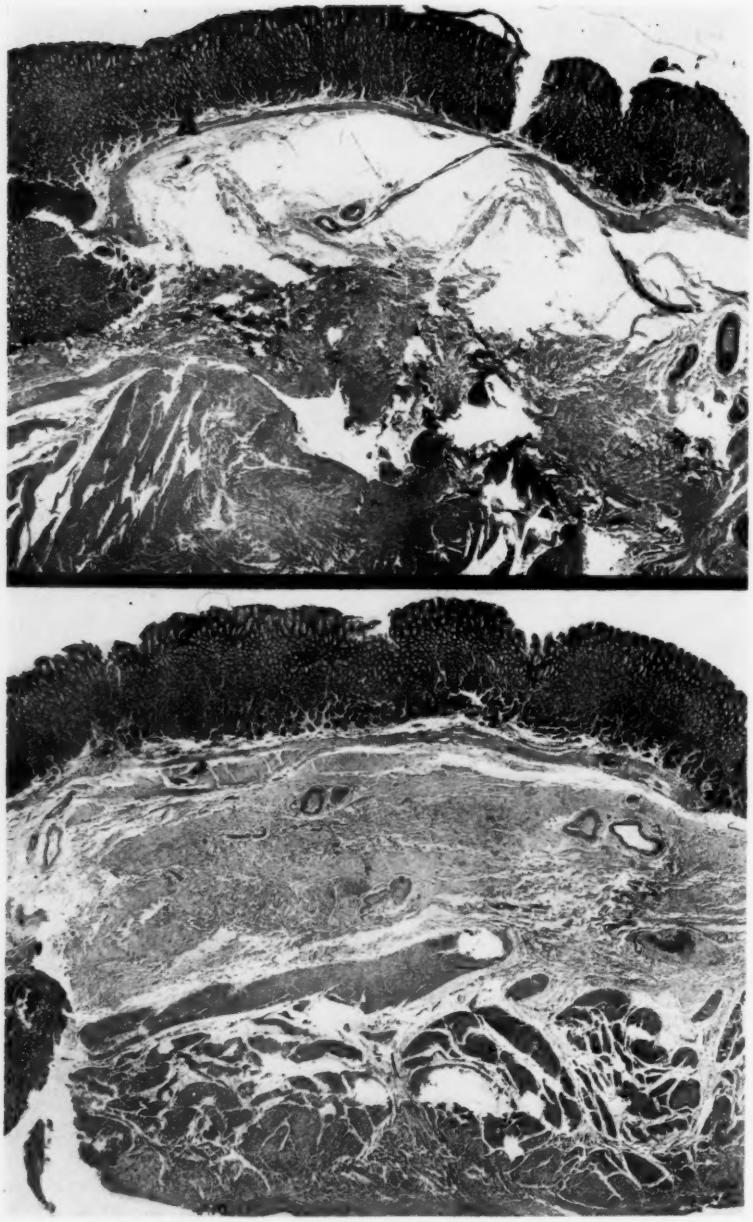


FIG. 4a.—Path. No. 75213: Original biopsy (Bouin fixed, low power). Note basal distortion in architecture (A) and edema of submucosa.

FIG. 4b.—Path. No. 75213: Post-resection biopsy (Bouin fixed, low power). Note small lymphoid aggregate above muscularis mucosae (B) and the increased edema and congestion of the submucosa. The septa of the muscularis propria are more edematous than those of Figure 4a.

are a few small aggregates of lymphocytes. The muscularis mucosae is thin and is not infiltrated by cellular elements.

The degree of congestion of the mucosa varies. Most of the capillaries of the papillae are small and of uneven caliber. They measure from one to four erythrocytes in width. Below the neck gland region only scattered capillaries, one erythrocyte in width, and a rare small venule, four erythrocytes in width, are present. Above the muscularis mucosae there are dilated congested venules, empty arterioles and small foci of hemorrhage near the lines of resection of the biopsy strips. Infiltrated collagenous tissue surrounds some of these arterioles and venules.

In the submucosa there are dilated, moderately congested arteries. The veins are more dilated and more congested. A small number of lymphocytes and an occasional eosinophil are found around some of the veins. The submucosal tissue is edematous. The septa of the muscularis propria are edematous and contain a small number of lymphocytes. The serosa is without significant change.

Postresection Biopsy.—Transitional Zone (see Fig. 4b): The formalin specimen consists of three strips that measure 0.7, 0.7, and 1 cm. in length, respectively; the Bouin specimen consists of four strips that measure 1, 1.2, 1.3, and 1.7 cm. in length, respectively.

The architecture of the mucosa corresponds to that of the original biopsy. The mucosal surface is covered by a narrow, and in places wide, layer of denser mucus which contains a few desquamated epithelial cells and many erythrocytes. The mucus is closely approximated to the surface cells, and in a few areas cannot be differentiated from the intracellular mucus. Scattered surface cells are flatter and contain less mucus than those of the original biopsy. Focally, the surface is more wavy than in the original biopsy specimen and the gastric area markings are more discernible.

The changes noted in the neck region and in the basal portions of the mucosa in the original biopsy are found here.

The state of the capillaries in the mucosa is similar. Near the muscularis mucosae there are a few more dilated veins. Most of these contain eosinophilic granular material. Some are filled with red blood cells. There are small foci of hemorrhage around the latter just above the muscularis mucosae.

The muscularis mucosae is focally wider than that of the original biopsy specimen. It presents a small amount of edema and an occasional lymphocyte.

The submucosa is more edematous. The larger, more dilated veins within it are filled with erythrocytes; the less dilated veins and the arteries contain eosinophilic granular material and a few erythrocytes. The septa of the muscularis propria are edematous and contain a few lymphocytes. The edema extends into the bundles of adjacent muscle fibers. The serosa is slightly edematous.

Case 5.—Path. 75330: Male, age 46, was admitted to the hospital in June, 1941. For the past year he was treated medically for a duodenal ulcer. One week prior to admission he experienced more severe epigastric distress, and during the past 24 hours noted hematemesis and melena. Wassermann—negative. Rehfuss' test meal—maximum free acid 60; maximum total acid 70.

The patient was prepared for operation with parenteral 5% glucose in physiologic saline. Magendie minims 6 and atropine gr. 1/150 were given hypodermically prior to anesthesia.

Operation.—June 16, 1941: Under spinal and intravenous sodium pentothal anesthesia, the stomach was found to be twice its normal size. Old and recent scar tissue and edema surrounded the first portion of the duodenum. An ulcer was found on its posterior wall penetrating into the pancreas. A small diverticulum projected from the greater curvature of the duodenum. Pathologic examination of the resected specimen disclosed a penetrating duodenal peptic ulcer.

The original biopsy specimen was taken 11 minutes after incision of the abdomen, from the anterior wall of the stomach in the antral region approximately two centimeters cephalad to the greater curvature. The resected specimen was removed 16 minutes later. Two minutes after removal of the specimen sections were taken from the edges of the original biopsy wound. Both biopsies were cut into strips one millimeter in width and placed in Bouin and formalin immediately.

Histology of the Biopsies.—*Original Biopsy—Antrum* (see Fig. 5a and 5b): The formalin specimen consists of two strips which measure 0.9 and 1.5 cm. in length; the Bouin specimen consists of two strips, each of which measures two centimeters in length.

The mucosal architecture of the major portion of each of the sections is considerably distorted by the disappearance of glandular elements and their replacement by cellular infiltration, bundles of smooth muscle fibers, and a small amount of collagenous tissue. The surface of the mucosa is wavy due to depressed, irregularly distributed, widened pits. It is covered in a few areas by narrow strands of mucus which contain rare desquamated epithelial cells and a few polymorphonuclear leukocytes.

The surface lining cells generally contain an average amount of mucus. Their nuclei vary in size, shape, staining intensity and position in the cell. The basal cytoplasm of many of the cells is narrow, elongated and separated from the neighboring cells by slit-like spaces that contain a small amount of eosinophilic, granular material. Vacuoles displace the basal cytoplasm and elevate the nuclei of a moderate number of the cells. A few larger vacuoles surround the nucleus completely and narrow the layer of supranuclear mucus. The vacuolization of the surface cells is similar over edematous and nonedematous papillae. Many of the basement membranes beneath the surface cells are widened and eosinophilic. These merge with eosinophilic, smooth material in the papillae or with the walls of underlying capillaries. In the Bouin-fixed sections the basement membranes are clearer and narrower, than in the formalin-fixed sections, despite the more easily discernible edema of the papillae in the former.

The majority of the papillae are edematous, moderately wide and infiltrated by numerous plasma cells; a few are nonedematous, narrow and minimally infiltrated. The pits contain degenerating polymorphonuclear leukocytes.

The neck portions of the glands are widely separated by extensive plasma cell and lymphocytic infiltration of the stroma, and in many areas are pushed aside, or replaced, by large masses of lymphocytes. The latter form diffuse aggregates or follicles in the middle third of the mucosa. Thick, hyaline collagenous fibers occur among the lymphocytes and concentrically surround portions of the periphery of the follicles. The long axes of the adjacent displaced neck glands are oblique. Many of the neck gland acini are dilated and contain polymorphonuclear leukocytes. Their lining cells are flattened, eosinophilic and contain irregular nuclei. Many of their basement membranes are indistinct and infiltrated by lymphocytes and a few polymorphonuclear leukocytes. A moderate number of argentaffine cells are found among the neck gland acini.

Large areas of the basal portions of the mucosa are completely replaced by dense masses of lymphocytes. These present a moderate number of secondary centers (follicle formation). They contain reticulum cells, dense, hyaline, collagenous fibers and groups of smooth muscle fibers. Some of the lymphoid aggregates occupy the lower third of the mucosa; others are so extensive that they reach the pit region. They enclose islands of degenerating glandular acini with vacuolated cytoplasm and deformed nuclei. Antral glands adjacent to the large lymphoid aggregates are pushed aside. Their long axes, originally perpendicular, are now almost parallel to the surface of the mucosa.

Between the masses of lymphocytes the relationship of the remaining antral glands to the muscularis mucosae and the stroma differs. The bases of a small number reach

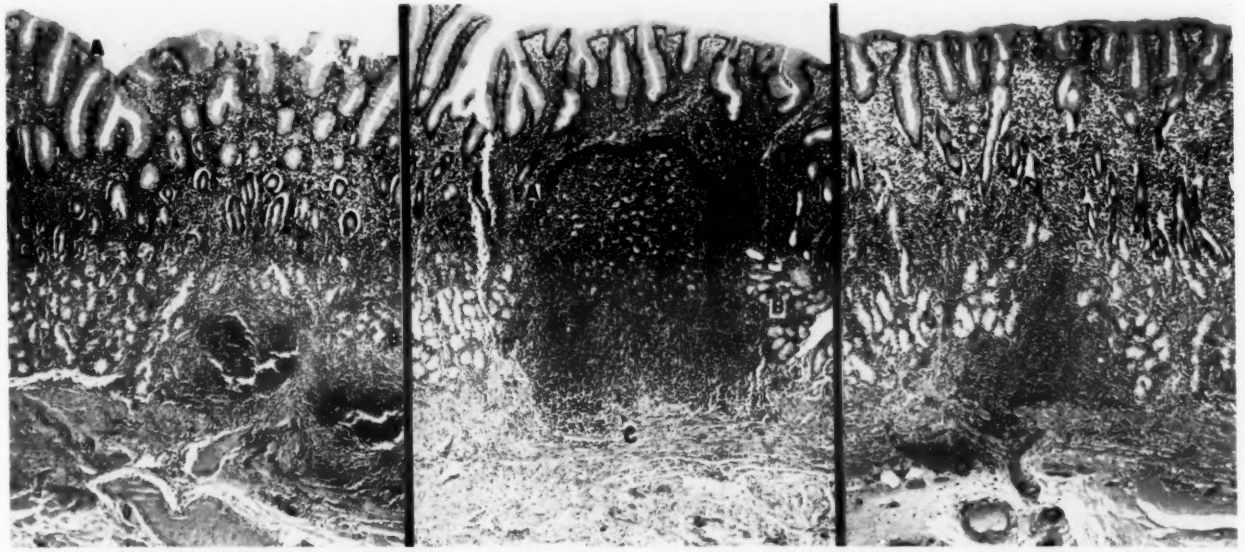


FIG. 5a.—Path. No. 75330: Original biopsy (Bouin fixed, magnification 62 times). Note the marked distortion of mucosal architecture and the basal lymphoid aggregates. Basal vacuolization of the surface cells (A). Small groups of acini (B) remain in the altered stroma.

FIG. 5b.—Path. No. 75330: Original biopsy (formalin fixed, magnification 62 times). Note complete replacement of antral and neck glands by large lymphoid follicle (atrophic infiltrative gastritis). The neck glands (A) and the antral glands (B) adjacent to the follicle are pushed aside. Their axes are changed. The muscularis mucosae (C) is infiltrated by lymphocytes.

FIG. 5c.—Path. No. 75330: Post-resection biopsy (Bouin fixed, magnification 62 times). The features are essentially similar to those described in Figure 5a. Note the greater amount of submucosal edema.

the muscularis mucosae; others are separated from the muscularis mucosae by a small amount of fine collagenous tissue infiltrated by lymphocytes, plasma cells and some eosinophils and polymorphonuclear leukocytes. Russell bodies are scattered through both this tissue and the areas of marked infiltration. In a few places above the muscularis mucosae the antral glands are replaced by dense collagenous tissue infiltrated by lymphocytes. The width of the muscularis mucosae is increased by moderate edema and lymphocytic infiltration. At some points beneath the large aggregates, lymphocytes replace the muscle fibers and destroy their continuity.

Congested capillaries, one to three erythrocytes in caliber, are noted at the summits of scattered papillae. A few capillaries, three to six erythrocytes in width, are at the level of the pit-neck junctions. The remainder of the mucosa is relatively bloodless. A rare small vein penetrates the muscularis mucosae. Within the latter there are some nondilated arterioles and venules filled with erythrocytes.

The submucosa is edematous and contains dilated arteries and veins filled with erythrocytes. A group of lymphocytes surrounds one vein. Lymphocytes from the large mucosal aggregates extend through the muscularis mucosae into the submucosa. The collagenous fibers superficial to the muscularis propria are denser than elsewhere and parallel to the mucosal surface.

The septa of the muscularis propria are slightly edematous. The serosa is without significant change.

Postresection Biopsy—Antrum (see Fig. 5c): The formalin specimen consists of four strips. Two of these each measure 0.8 cm. in length; the other two each measure 2.5 cm. in length. The Bouin specimen consists of four strips which measure 0.6, 0.8, 1.3, and 1.6 cm., respectively.

The mucosal architecture corresponds closely to that of the original biopsy.

The surface of the mucosa is covered by narrow and wide layers of denser mucus which contains desquamated epithelial cells, erythrocytes and single and clumped polymorphonuclear leukocytes. In some areas the mucus merges with the intracellular mucus of the surface cells so that but a narrow, eosinophilic zone of cytoplasm remains. This is either anuclear, or contains a deformed, shrunken or swollen, poorly demarcated nucleus. The boundaries between the surface cells in these areas are not distinguishable. Erythrocytes and lymphocytes in greater numbers are found between and within the surface cells than in the original biopsy. More of the surface cells are basally vacuolated but the degree of vacuolization is similar

The pits are slightly longer. In the neck glands a few regular mitoses are present. The argentaffine cells are slightly more numerous.

The type and degree of infiltration and the alteration of the neck and antral glands correspond to that of the original biopsy. The eosinophils in the muscularis mucosae are slightly more numerous. The edema of an occasional papilla is greater Focally, there is greater edema above the muscularis mucosae and between groups of its muscle fibers. The remaining coats of the gastric wall are more edematous.

Congested capillaries at the summits of the papillae are more numerous but are of the same caliber (one to three erythrocytes in width). At the pit-neck junctions, congested capillaries three to six erythrocytes in width, and congested venules eight to ten erythrocytes in width are more numerous. The deeper portions of the mucosa, as in the original biopsy, are relatively bloodless except for an occasional perpendicular congested venule (six to eight erythrocytes in width) which runs superficially from the muscularis mucosae. A few venules, three erythrocytes in width, and a few contracted arterioles are present above the muscularis mucosae. The submucosal veins and the capillaries of the septa of the muscularis propria are more congested. Focal hemorrhage occurs in the submucosa and the septa of the muscularis propria.

COMMENT

A study of Table III demonstrates quite clearly and conclusively that the fundamental histologic architecture of the biopsy specimens taken prior and subsequent to resection was not essentially altered by the operation of subtotal gastrectomy *per se* in any of the 35 cases which were analyzed. It should be remembered, however, that the number and distribution of the infiltrating cells varied in many of the biopsy strips from the same specimen, but such differences in adjacent mucosal areas have been found to be common.

However, the surgical procedure did produce changes in the surface of the mucosa, alterations in the amount of tissue fluid throughout the entire gastric wall, and congestion of the blood vessels. The amount of surface mucus increased and the volume of intracellular mucus decreased as the interval lengthened between the original biopsy and the resection of the specimen. In a few instances in which this interval exceeded 20 minutes, the intracellular mucus merged with that on the surface. However, the loss of this intracellular mucus rarely produced significant cytoplasmic or nuclear changes in the surface cells. Minor changes in the shape and height of the papillae and in the width and contour of the pits were observed. When alterations of the surface cells, including basal vacuolization, focal pseudostratification (piling), variation in the position, shape and staining intensity of the nucleus were noted in the original biopsy, they were also present in the postresection specimens. In some of these cases there were small numbers of polymorphonuclear leukocytes around the neck glands or in the papillae in the postresection biopsies.

Stromal edema and capillary congestion of the papillae, and edema of the stroma superficial to the muscularis mucosae were more evident in the postresection biopsy, except in one case (Case No. 75918), in which the basal edema was less intense. Generally, the muscularis mucosae was more edematous. It should be noted that the edema was most striking in the submucosa and in the adjacent septa of the muscularis propria when the interval between the biopsies exceeded 20 minutes.

Hemorrhage involving the entire mucosa occurred mainly near the edges of the original biopsy. This was present regardless of the time interval between the original biopsy and the resection. The glandular acini were separated by the extravasated blood but remained intact except in No. 70421, in which desquamation of the antral cells was present. In No. 76566 a small number of surface cells were destroyed over one hemorrhagic papilla. Submucosal hemorrhage was more striking and most marked when the intervals exceeded 20 minutes. The hemorrhage involved mainly those portions of the submucosa just beneath the muscularis mucosae and above the muscularis propria. In Case 1, Path. No. 70308, in which but ten minutes elapsed between the original biopsy and the resection, the submucous hemorrhage was quite extensive. The veins of the submucosa, and the capillaries and venules of the septa of the muscularis propria were more congested in the postresection

biopsy. The walls of some of these vessels were infiltrated and surrounded by polymorphonuclear leukocytes.

CONCLUSIONS

1. No histologic differences of diagnostic significance were found in this series of 35 cases in which preliminary and postresection biopsies were carefully studied and compared.

2. Postresection specimens, if fixed immediately, represent, with minor modifications, the histologic state of the gastric wall existent prior to resection.

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THE EFFECT ON GASTRIC ACIDITY OF GASTRO-ENTEROSTOMY AND GASTRIC RESECTION FOR PEPTIC ULCER*

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IT IS IMPORTANT TO KNOW, if possible, the underlying reasons for performing gastro-enterostomy and gastric resection for peptic ulcer. Particularly in a teaching clinic, engaged in training young surgeons, we should know why we advocate the surgical methods which we teach and how they achieve their effects. I need not, before this audience, take the time to discuss the reasons commonly advanced to explain why these procedures are effective or why they fail. In more recent years, as you are aware, the etiologic relationship between excessive acid and ulcer has been emphasized through the experimental and clinical work of Dragstedt, Wangensteen, and many others, whose important work deserves more consideration than can be given it in so short a presentation. As a result of this work some authors believe that the empiric surgical approach to the problem of ulcer in man can be abandoned and may now be approached scientifically on the basis that the acid secreted by the stomach is the important factor in the causation of ulcer. Surgical procedures, therefore, which abolish or diminish acid gastric secretion may be expected, on this basis, to cure ulcer and prevent recurrence. It has been observed by a number of authors that gastro-enterostomy fails to alter acid secretion. It does not, therefore, to many, meet the requirements of a surgical operation designed to cure ulcer, even though there is abundant evidence in the literature that it relieves the symptoms and protects the individual against the complications of ulcer in a fairly high percentage of cases. It has also been observed that gastric resection, if of sufficient magnitude, does diminish or abolish acid secretion and, therefore, more nearly meets the requirements of an ideal operation for the cure of ulcer. Certain authors have gone farther in their approach to the problem and find that not only resection, but specific types or methods of resection assure achlorhydria more certainly than others. Thus, for example, Wangensteen has found that with a resection of three-fourths of the stomach, and according to the Hofmeister or Finsterer exclusion method (the latter with excision of antral mucosa), 63 per cent of his patients are achlorhydric, and fail to develop gastrojejunal ulcer.

It will be observed that the recent emphasis has been laid upon actual reduction or diminution of acid secretion by the removal of secretory gastric mucosa. The factors of dilution and neutralization of acid through surgical procedures—another possible explanation for their success if acid is the

* Read by title before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

important factor in the causation of ulcer—have not recently received much attention. Yet Dragstedt, and others, have shown that food, pancreatic juice, gastric and intestinal mucus, duodenal juice and bile, dilute and neutralize the acid and together probably account for the fact that the stomach does not constantly digest itself. There seems no reason to believe that successful dilution and neutralization of acid may not be as effective a means of combatting ulcer as actual reduction in acid. In gastro-enterostomy we know that postoperatively the acid gastric secretion is only rarely significantly reduced; yet the operation, in our hands and in the hands of many others, gives satisfactory results over a long-term follow-up period in 75 to 80 per cent of cases. In gastric resection the changed conditions created are much the same as in gastro-enterostomy. There is an artificial stoma without sphincteric control, opportunity for rapid emptying of the stomach, possibility of regurgitation of alkaline intestinal contents and, therefore, of dilution and neutralization of acid. The removal of acid-secreting mucosa, the result of resection, may well be an added advantage of the operation, in that it may reduce the total volume of acid secreted. But the factor of dilution and neutralization remains as a reason for the beneficial effects of resection and it is possible that the effect of reduction of acid has been overemphasized. The matter has more than academic interest. The idea that acid is the important factor in the genesis of ulcer may be sound; but the idea of controlling the production of acid by larger and larger resections has already led us to sacrifice the greater part of an often normal organ without solving the problem of ulcer; and with a mortality which must be considered. We believe that the subject warrants further study.

In the course of a study of some 1200 patients with peptic ulcer admitted to our wards in the past ten years, we have assembled those patients who have been subjected to operation and who have had careful pre- and postoperative acidity determinations made. The determinations all have been made by the junior author and according to the histamine method of Bloomfield and Polland. Only patients in whom the junior author is satisfied that both pre- and postoperative acidity determinations are above reproach are included in this presentation. The determinations extend over a period up to seven years after operation, and in many cases have been repeated over the years. The credit for this work belongs, then, to the junior author; the senior author having merely collected and tabulated the data and drawn such conclusions as seemed justified. The purpose of the study has been (a) to determine the effect of gastro-enterostomy and gastric resection upon acid secretion; (b) to determine the acid secretion according to the magnitude of gastric resection; (c) to determine the results of operation in relation to the postoperative acid secretion; and (d) to determine the results of operation regardless of the acid secretion.

I. GASTRO-ENTEROSTOMY

Seventy-five patients with gastro-enterostomy for gastric and dudenal ulcer, the latter predominating, have been studied. In all the pre- and post-

operative acidity determinations are satisfactory and reliable. The results are shown in Charts 1 and 2. In Chart 1, showing the postoperative acidity determinations following gastro-enterostomy, it is observed that of the 75 patients, 69 or 92 per cent, show free hydrochloric acid equal to and, in the large majority, greater than normal (60° free HCl); while but six, or eight per cent, have acidities below normal. The average postoperative acidity for the 75 patients is 82° free HCl. In Chart 2, showing the pre- and postoper-

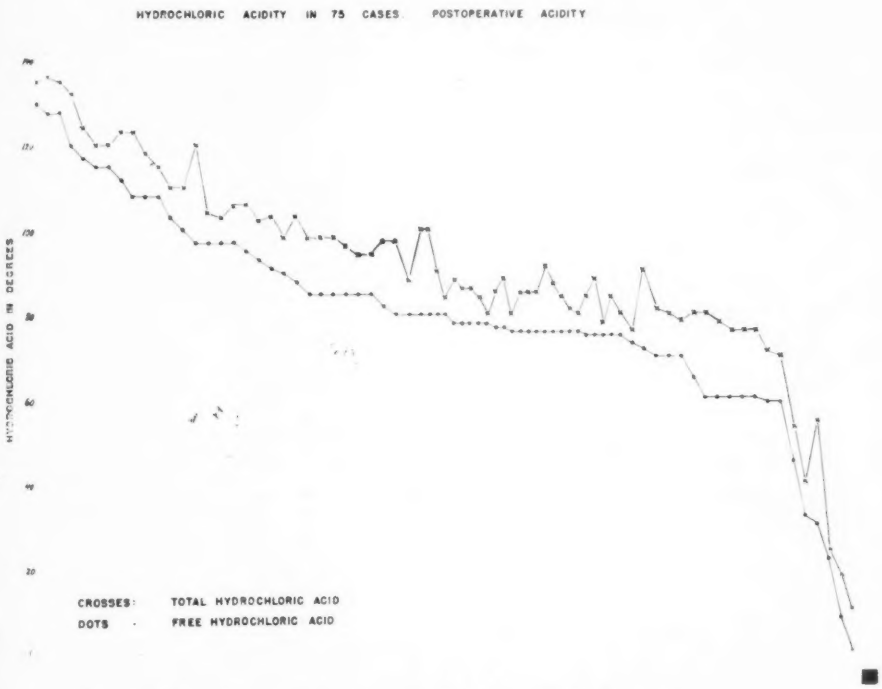
HYDROCHLORIC ACIDITY IN 75 CASES POSTOPERATIVE ACIDITY
HYDROCHLORIC ACID IN DEGREES
CROSSES: TOTAL HYDROCHLORIC ACID
DOTS . FREE HYDROCHLORIC ACID

CHART I. Determinations of gastric acidity in 75 patients after Gastroenterostomy.

ative acidities of 50 patients particularly and repeatedly studied, it will be observed that in 28, or approximately one-half of the cases, the preoperative acidity is slightly higher than the postoperative; in 22, the postoperative acidity is higher than the preoperative. In only five patients is there a significant diminution in acidity following operation. The average preoperative acidity for 50 patients is 90° free HCl; excluding the five patients, the average postoperative acidity is 88° free HCl. In the series, the interval of time between operation and postoperative gastric analysis does not appear strikingly to influence the findings; although it should be said that for the majority of patients the interval between operation and the last gastric analysis is less than five years. Regardless of the manner in which the clinical results are compared with the acidity, there does not appear to be any correlation between them. Of the 75 patients studied, 56, or 75 per cent, after a period of follow-up of from six to ten years, have satisfactory results following

gastro-enterostomy; and in the presence of postoperative acidities which vary between 0° and 132° free HCl. Nineteen, or 25 per cent, have unsatisfactory results, and in the presence of acidities which vary between 50° and 130° free HCl.

From a study of these 75 patients, then, it would appear that gastro-enterostomy affects the acid secretion of the stomach only in exceptional cases. Moreover, it appears that the satisfactory and unsatisfactory results

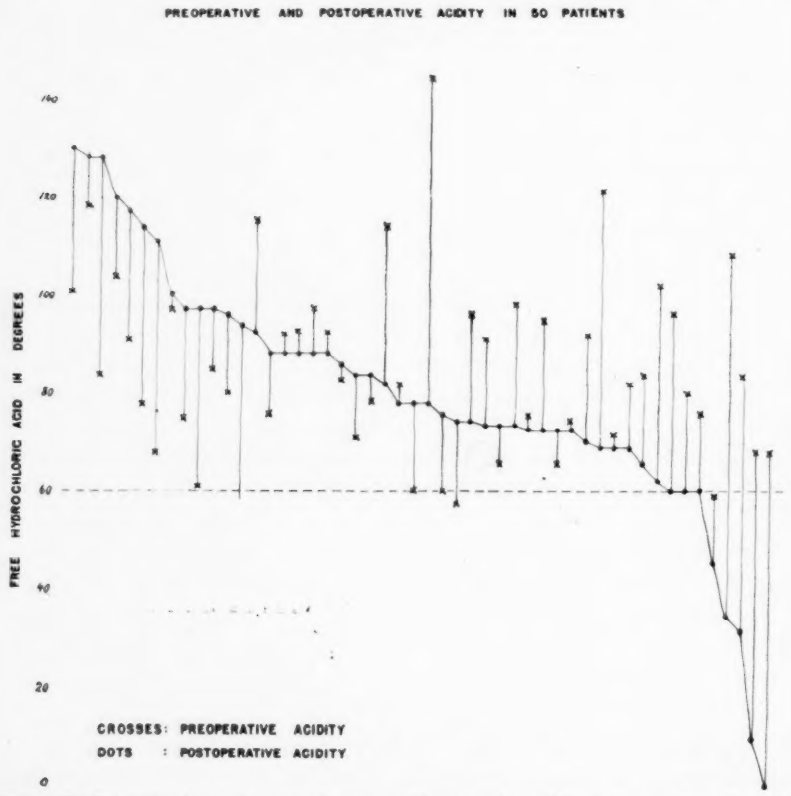

CHART II. Determinations of pre and postoperative gastric acidity in 50 patients treated by Gastroenterostomy.

following operation can not, to any considerable degree, be related to the secretory activity of the stomach. If a high acid is the important etiologic factor in the genesis of ulcer and the cause of its perpetuation or its recurrence, then gastro-enterostomy achieves its results probably by more rapid and complete dilution and neutralization of acid.

II. GASTRIC RESECTION

Eighty-eight patients with gastric and duodenal ulcer subjected to gastric resection have been studied. Of these, 63 had duodenal and 25 gastric ulcers. They were subjected to resection of varying magnitudes. Thirty-one patients had what may be called a mininal resection—less than one-half of the

stomach but including the antrum, pylorus and ulcer bearing duodenum—46 patients had what may be termed a moderate resection—one-half to two-thirds of the stomach—and 11 patients had a major resection—over two-thirds to three-quarters of the stomach, or more. The results of these resections, which were chiefly according to the Billroth-II, Pólya or Hofmeister methods, are shown in Tables I, II and III, and are summarized as follows:

TABLE I

THE EFFECT OF GASTRIC RESECTION IN RELATION TO ACID GASTRIC SECRETION IN 63 PATIENTS WITH DUODENAL ULCER HAS BEEN A POSTOPERATIVE ANACIDITY IN 17, OR 27 PER CENT, A LOW ACID (BELOW 60° FREE HCL) IN 15, OR 23.8 PER CENT, AND NO SIGNIFICANT CHANGE IN ACIDITY (60° FREE HCL OR MORE) IN 31, OR 49.2 PER CENT. THE THREE GROUPS WITH ANACIDITY, LOW ACID, AND NO CHANGE IN ACID, ARE ANALYZED AS FOLLOWS:

GROUP I. 17 PATIENTS HAVING A POSTOPERATIVE ANACIDITY, OR ACHLORHYDRIA

Extent of Resection	Number of Cases	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach	0		
½ to ⅔ of stomach	16	14 (87.5%)	2 (12.5%)
Over ⅔ to ¾ or more	1	1 (100.%)	

GROUP II. 15 PATIENTS HAVING POSTOPERATIVELY A LOW ACIDITY

Extent of Resection	Number of Cases	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach	4	4 (100.%)	
½ to ⅔ of stomach	9	9 (100.%)	
Over ⅔ to ¾ or more	2	2 (100.%)	

GROUP III. 31 PATIENTS HAVING POSTOPERATIVELY AN ADEQUATE OR HIGH ACIDITY

Extent of Resection	Number of Cases	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach	21	18 (85.7%)	3 (14.3%)
½ to ⅔ of stomach	9	7 (77.7%)	2 (22.3%)
Over ⅔ to ¾ or more	1	1 (100.%)	

TABLE II

THE EFFECT OF GASTRIC RESECTION IN RELATION TO ACID GASTRIC SECRETION IN 25 PATIENTS WITH GASTRIC ULCER HAS BEEN A POSTOPERATIVE ANACIDITY IN 18, OR 72 PER CENT, A LOW ACID IN FIVE OR 20 PER CENT, AND NO CHANGE IN ACIDITY IN TWO OR EIGHT PER CENT. THE THREE GROUPS WITH ANACIDITY, LOW ACID, AND NO CHANGE IN ACID ARE ANALYZED AS FOLLOWS:

GROUP I. 18 PATIENTS HAVING A POSTOPERATIVE ANACIDITY

Extent of Resection	Number of Cases	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach	2	2 (100.%)	
½ to ⅔ of stomach	9	9 (100.%)	
Over ⅔ to ¾ or more	7	7 (100.%)	

GROUP II. 5 PATIENTS HAVING POSTOPERATIVELY A LOW ACID

Extent of Resection	Number of Cases	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach	2	2 (100.%)	
½ to ⅔ of stomach	3	2 (66.6%)	1 (33.3%)
Over ⅔ to ¾ or more	0		

GROUP III. 2 PATIENTS HAVING POSTOPERATIVELY NO CHANGE IN ACIDITY

Extent of Resection	Number of Cases	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach	2	2 (100.%)	
½ to ⅔ of stomach	0		
Over ⅔ to ¾ or more	0		

TABLE III

SUMMARY OF TABLES I AND II—88 PATIENTS WITH DUODENAL AND GASTRIC ULCER

Extent of Resection	Number of Cases	Number with Anacidity	Number with Low Acidity	Number with Normal or High Acidity	Satisfactory Clinical Results	Unsatisfactory Clinical Results
Less than ½ of stomach.....	31	2 (6.4%)	6 (19.3%)	23 (74.3%)	28 (90.3%)	3 (9.7%)
½ to ⅔ of stomach.....	46	25 (54.3%)	12 (26. %)	9 (19.6%)	41 (89.1%)	5 (10.9%)
Over ⅔ to ¾ or more.....	11	8 (72.7%)	2 (18.1%)	1 (9.2%)	11 (100.%)	

(a) Of 31 patients with minimal gastric resections, eight, or 25.7 per cent, show postoperatively a low acidity (less than 60° free HCl), of whom two have an anacidity; while 23, or 74.3 per cent, have an adequate or high acidity (60° free HCl, or more). The follow-up of these 31 patients shows that 28, or 90.3 per cent, have satisfactory results, three, or 9.7 per cent, have unsatisfactory results.

(b) Of 46 patients with moderate resection, 37, or 80.4 per cent, show postoperatively a low acidity, of whom 25 have an anacidity; while nine, or 19.6 per cent, have an adequate or high acidity. The follow-up of these 46 patients shows that 41, or 89.1 per cent, have satisfactory results, five, or 10.9 per cent, have unsatisfactory results.

(c) Of 11 patients with major resection, ten, or 90.8 per cent, show postoperatively a low acidity, of whom eight have an anacidity; while one, or 9.2 per cent, has an adequate acidity. The follow-up on these 11 patients shows that all, or 100 per cent, have satisfactory results.*

Although the number of major resections is too small to be conclusive, the above findings indicate (a) that gastric resection does reduce acid gastric secretion, and in direct proportion to the extent of the resection; and (b) that patients with postoperative low acidity, or anacidity, have, as a group, had better results by ten per cent than those with an adequate or high acidity.

But the study shows, also, that the satisfactory results from resection do not parallel the gastric acidity. The results of minimal resection, following which only 25 per cent of patients have an acidity below normal, are as good as those of moderate resection, following which 80 per cent of patients have an acidity below normal. The results of major resection, following which 90 per cent of patients have a low acidity, are better than those of minimal and moderate resection in the small group of 11 patients here presented; but I feel reasonably sure will not prove to be when we include the major resections of those patients whose results we know, but whose acidity studies have not been completed. Again, if we compare the results in all patients who, postoperatively, have a low acidity, with the results of minimal, moderate and major resections, regardless of the resulting acidity, we find that they approach within five per cent of each other.

It would appear then, from our experience, (1) that subtotal gastric resection, of whatever magnitude or method, does not ensure an achlorhydria; (2) that the beneficial effects of gastric resection are not necessarily

* Of the 88 patients with gastric resection, 50 have been followed one to two years; 30, two to five years, and eight, five to ten years.

due to the reduction in acid secretion but commonly are obtained, as in gastro-enterostomy, in the absence of significant change in acidity; and (3) that the chances of ensuring either achlorhydria, or significantly better results, by increasing the magnitude of resections beyond a moderate resection are rather small. There are objections to major resection. The mortality in the hands of the majority of surgeons is rather high. It does not prevent recurrent ulceration, particularly in duodenal ulcer, and it makes difficult and hazardous any further surgery if recurrent ulceration takes place.

SUMMARY AND CONCLUSIONS

1. A study of the pre- and postoperative acidities in 163 patients with peptic ulcer subjected to gastro-enterostomy or gastric resection shows that, postoperatively, 61, or 37.4 per cent, have achlorhydria or low acidity, while 102, or 62.6 per cent, have an adequate or high acidity. In the presence of these acidity findings, 136, or 83.4 per cent, of the patients have satisfactory clinical results. This lack of correlation between acidity and results leads us to doubt that a reduction in acid secretion is the sole factor in achieving the results in these two types of operation.

2. Following gastro-enterostomy there is no significant change in acid secretion; yet in this series of 75 patients, 75 per cent have satisfactory results over a follow-up period of six to ten years. It must be presumed that dilution and neutralization of acid rather than reduction in acid is the effective means of achieving these results, if acid is the important factor in the genesis of ulcer.

3. Following gastric resection there is, in general, a reduction in acid secretion in proportion to the extent of the resection. But resection of any magnitude, consistent with a reasonable mortality, does not, in our experience, ensure achlorhydria. Moreover, when we compare the clinical results with the acidity, we again find a lack of correlation; for in minimal resection, as above described, 90 per cent of the patients have satisfactory results, while 25 per cent have a reduction in acid. It is probable that in resection, also, dilution and neutralization of acid are important factors in the results obtained.

4. If these findings are confirmed by others, it would appear of doubtful value to pursue the idea of ensuring achlorhydria and, therefore, better results by larger and larger resections. It may be better to accept the limitations of resection as a treatment of ulcer and adopt an operation of lesser magnitude which ensures fairly satisfactory results with a reasonable mortality and permits further surgery if recurrence takes place.

5. The findings presented do not controvert the etiologic relationship between acid and ulcer. It is possible that operations other than those discussed, which are now being tested in our department, may not only support the present evidence of this relationship but achieve a reduction in acid more constantly than does gastric resection.

CHOLECYSTO-ENTEROSTOMY, CHOLEDOCHO-ENTEROSTOMY AND ENTERO-ENTEROSTOMY BY MEANS OF RUBBER BANDS: THE USE OF RUBBER BANDS IN THE MIKULICZ OPERATION*

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AND

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A special rubber cord was used by Theodore A. McGraw[1] more than 50 years ago in gastric and intestinal surgery. The stomach wall is thick and not very satisfactory for this technic. The contents of the stomach and upper small intestine usually have but few bacteria, and an adequate communication between them can best be made by incision and suturing. However, there seems to be a place for a practically aseptic closed technic in which an opening can be established between viscera with highly septic contents. If this can be done with ordinary rubber bands instead of special elastic cords and special instruments, it would seem desirable.

We have performed nine experiments upon dogs, anastomosing the limbs of a loop of small bowel to each other or the small bowel to the cecum. In two experiments, after 24 hours there was slight necrosis of the tissue, and in one, a small fistulous opening. After 48 hours there was a larger fistulous tract. In other dogs, after two weeks, there were no symptoms of obstruction even when the loop of bowel between the application of the band was occluded. In three of the experiments the rubber band was surrounded with catgut suturing. In six there was no suturing; the band alone was used. In none of the experiments was there any evidence of peritonitis or leakage.

Fig. 1.—This drawing shows the needle threaded with No. 32 stationer's rubber band cut obliquely. The needle and band are dipped in a solution of iodine just before being used. The end is then clamped with hemostatic forceps so that the band can be applied under tension.

In both experimental and clinical work the ordinary stationer's No. 32 rubber band is cut obliquely and threaded into a large, curved needle without a cutting point, formerly called a catgut needle (Fig. 1). Two segments of bowel, or the bowel and the gallbladder, are first united with a continuous suture of fine chromic catgut (Figs. 2 and 8). The rubber band with the needle is dipped into iodine solution just before being used. A long, deep bite is taken in one loop of the viscus. The end of the band is clamped with a hemostat. The band is drawn through under considerable tension. A second bite is taken in the apposing viscus in the opposite direc-

* Read by title before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

tions (Figs. 3 and 9). A bite of three to five centimeters may be easily obtained by puckering the bowel so the needle can catch a much longer bite than if the bowel were held smooth (Fig. 8).

While in six experiments there was no suturing and no leakage, clinically, it seemed safer, and added very little to the time and difficulty of the operation, to surround the band with a continuous suture of fine chromic catgut. In the clinical cases, also, there has been no leakage. In all of the clinical cases the band has been reinforced by suturing. In two patients upon whom an entero-enterostomy was performed, and the patients died from other causes, it was found that the band had not cut through in one case, Mr. A. F. D. (Case No. B-8307), eight days after operation; and there was only a very small opening between the loops in another case, Mr. W. P. M. (Case No. B-9726), 11 days after operation. In these two cases only a single band was used. In one other case, Mrs. N. G. N. (Case No. C-2415), the triple band technic was used to by-pass a small segment of bowel injured by a femoral hernia. The bowel was not gangrenous. The second and third bands were very small and no incision in the peritoneum embraced by the rubber band (as is now done) was made. Four days later there was obstruction; the loop of bowel with the bands was resected and the patient recovered satisfactorily. The specimen showed the bands had not cut through. Although this was only four days after the operation it was contrary to our experience in the experimental work, for in all of the dogs after 48 hours there was a fistulous tract between the apposed bowels, though in some it was rather small. Therefore, we modified the clinical procedure, for it was apparent that when the apposing walls of viscera are brought together by the rubber band, tissue is compressed with the peritoneal surfaces in intimate contact. This makes for strong union of the portion of bowel within the grasp of the band and the compressed tissues heal together firmly and solidly and may offer such resistance that a fistulous opening does not form.

The technic as now employed is as follows: The apposing viscera are united with a row of continuous sutures of fine chromic catgut (Figs. 2 and 8). A No. 32 rubber band is passed, as described, while sufficient tension is made on the band to reduce its size. If the end of the band is clamped and firmly held while the band is being passed under traction, when the traction is released, the band enlarges, fills the needle hole, and prevents leakage. This makes the procedure practically aseptic. In one case, the anastomosis was made with the gallbladder and, when fine chromic catgut sutures were passed between the gallbladder and the bowel, there was slight leakage of bile, though when the band was passed through the bowel and the gallbladder there was no leakage. The rubber band is carried through the viscera to be united, but it is not tied (Figs. 3 and 9). Then a second No. 32 rubber band, in the same type of needle is passed through the bite in the bowel made by the first band on one side and a third band is similarly passed on the opposite side. An in-

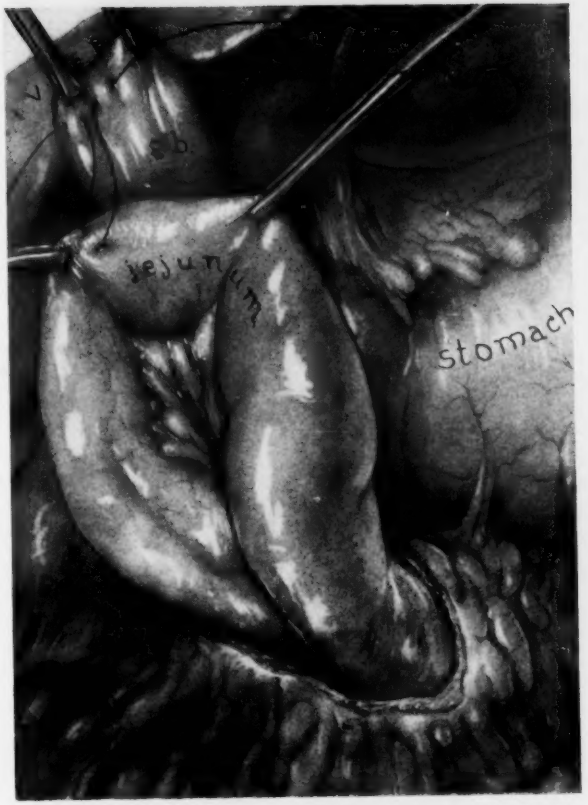

FIG. 2.—The first step in cholecystojejunostomy: A loop of jejunum about two feet from its origin is brought through the transverse mesocolon. If the transverse mesocolon is short and fat, it can be brought over the transverse colon. The jejunum is fastened to the gallbladder with a continuous suture of fine chromic catgut.

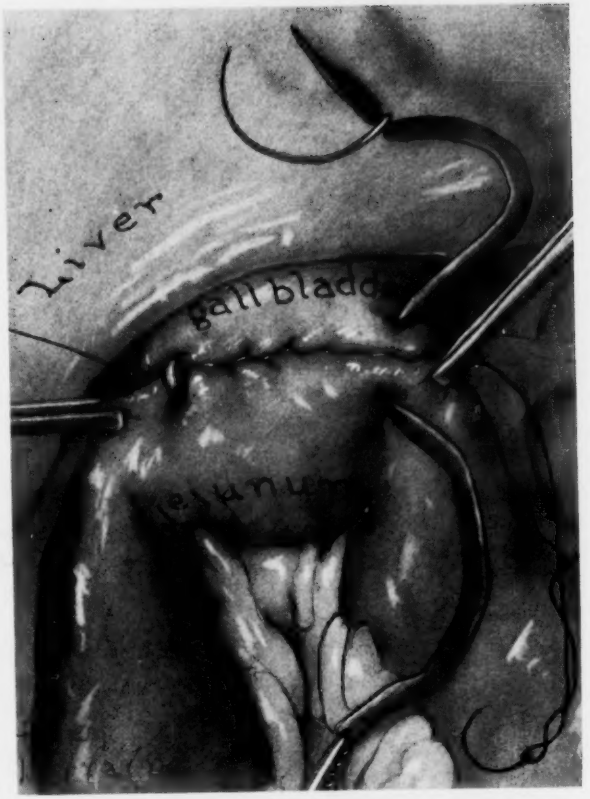

FIG. 3.—A No. 32 rubber band is passed first through the jejunum and then in a reverse direction through the gallbladder.

fat, it can be brought over the transverse colon. The jejunum is fastened to the gallbladder with a continuous suture of fine chromic catgut.

FIG. 4.—Before tying this band, however, two other bands are passed—one through the portion of jejunum that is embraced in the bite of the first band and a third band catching the portion of the gallbladder that the first band embraces. An incision is made in the jejunum through the peritoneum and a portion of the muscular coat, taking care not to penetrate the lumen of the bowel. The third band which has been applied to the gallbladder is tied snugly without the necessity of incising the peritoneum.

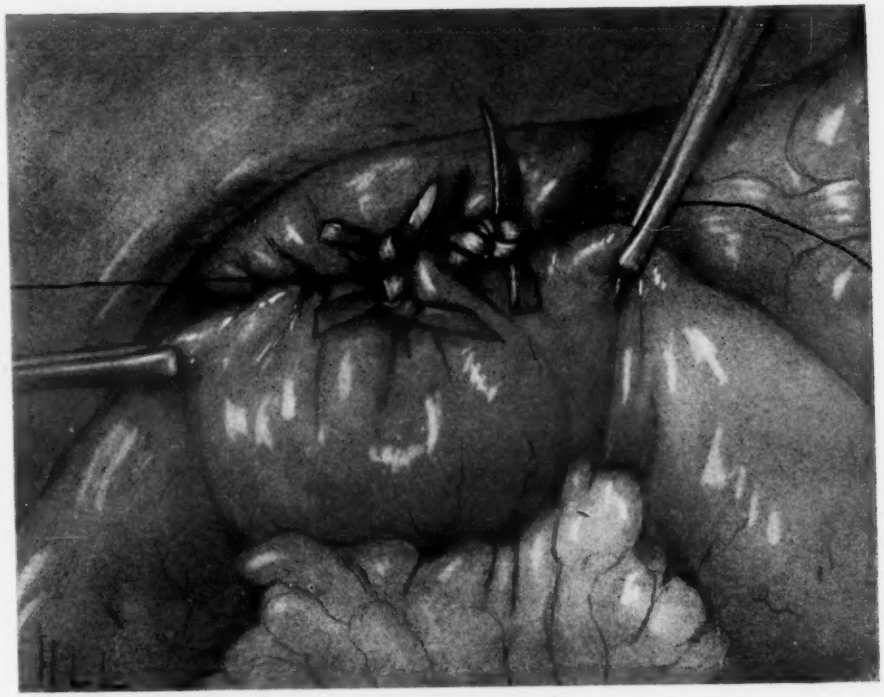

FIG. 5.—All of the bands have been tied tightly and the posterior suture is taken up.

cision is made through the peritoneum and some of the muscular coat of that portion of the bowel within the grasp of the last two bands and each of these bands is tied down snugly (Figs. 4 and 10). Then the first band is tied several times very tightly (Figs. 5 and 11). The suturing around the rubber band is completed (Fig. 6).

In this manner the situation as regards compression of the apposing surfaces is materially altered. Instead of having two peritoneum-covered surfaces approximating each other under heavy pressure, with the optimum conditions for stout union, the inner rubber bands prevent this union, not

FIG. 6.—The posterior suture has been completed anteriorly and is tied to its original end. In addition, a series of interrupted mattress sutures is placed. The ends are left long and a tag of omentum or peritoneum-covered fat is carried around the anastomosis and fastened in position by passing through it the long ends of the mattress sutures.

only by preventing approximation of the peritoneum of the apposing viscera, but their own compression in each loop of the viscera makes independent openings. The incision in the peritoneum also aids in establishing an opening. In the triple rubber band technic suturing is essential.

From May 15, 1941 (the first case) to January 1, 1943, the rubber band operation has been performed 19 times on 18 patients. The technic with a single rubber band was used in nine operations, and with the triple rubber bands in ten operations. In all of the recent cases the triple rubber bands have been employed.

The indications for this operation may be classified under four heads: (1) *For obstruction of the terminal portion of the common duct:* When

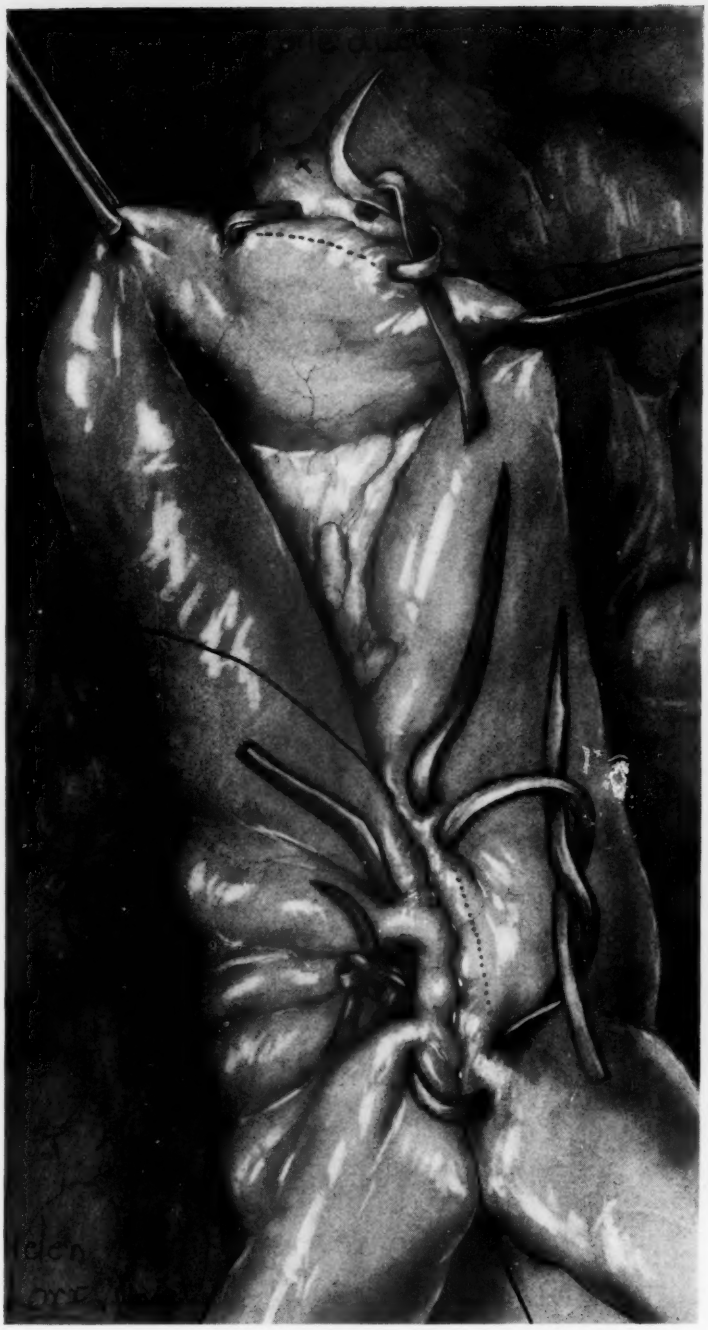

FIG. 7.—Choledochojejunostomy. The jejunum has been sutured to the common bile duct. A rubber band has been passed through the apex of the loop of jejunum and in a reverse direction through the common bile duct. Along the dotted line an incision through the peritoneum and part of the muscular coat of the bowel is made. The rubber band is tied down tightly and the suture is taken up, carried forward and tied to its original end. Interrupted mattress sutures of fine chromic catgut are placed and omentum or peritoneum-covered fat is brought around and fastened as in the cholecystojejunostomy. The lateral anastomosis or entero-enterostomy is in a stage of completion. The first rubber band has been placed. The second and third rubber bands are also in position. The peritoneum and superficial portion of the muscular coat are incised along the dotted line. On the left this incision has been made and one of the rubber bands has been tied. The rubber band on the right side is to be tied and then the first rubber band is tied snugly. The continuous suture is carried forward and tied to its original end.

the obstruction is from a calculus, the stone should be removed even though the duodenum must be incised, and this usually suffices. But in obstruction from a malignant growth in the head of the pancreas or in the ampulla of Vater, when a radical operation does not appear wise; or in obstruction from a benign lesion, such as a stricture, this procedure is indicated. However, it is subdivided into (a) cases in which the gallbladder is present (Fig. 2); and (b) cases in which the gallbladder has been previously removed (Fig. 7). We have had cases under both of these subheads.

(2) *Intestinal obstruction.*

(3) *Entero-enterostomy as an adjuvant to anterior gastro-enterostomy or to total gastrectomy.*

(4) *In the Mikulicz-type of operation.*

(1a)—In terminal obstruction of the common duct when the gallbladder is present and its exploration is desired, the gallbladder may be emptied with a trocar and cannula, incised, and explored with the finger. The incision is closed with a purse-string suture and the technic is then applied as though the gallbladder had not been opened. The exploration may be unnecessary. The excellent procedure of Brunschwig,[2] who, in excision of the duodenum or head of the pancreas for cancer, brings over a loop of jejunum and anastomoses it with the gallbladder, is employed. A loop of jejunum is selected at a distance of about two feet from the origin of the jejunum so there can be no kink or tension. The loop is brought either over the transverse colon or through the mesocolon and fastened to the gallbladder with a continuous suture of fine chromic catgut (Fig. 2). With the thin wall of the gallbladder and only a small opening needed, probably a single rubber band is all that may be necessary, but the three-band technic provides a larger fistula. The band is inserted through the apex of the loop of the bowel, catches a bite of about two centimeters, and then is passed through the gallbladder in the opposite direction (Fig. 3). The peritoneum of the bowel is incised and the band is tied very tightly (Figs. 4 and 5). The row of sutures of fine chromic catgut is again taken up and continued anteriorly, burying the band (Fig. 6). A few interrupted mattress sutures of fine chromic catgut are placed and the ends are left long. A tag of omentum or peritoneum-covered fat is carried around the anastomosis, and the ends of these sutures are passed through the peritoneum-covered fat and tied firmly. At the base of the loop an entero-enterostomy is made by three rubber bands.

We have had two cases of benign obstruction in which this was done, with very satisfactory recovery, and clearing up of the jaundice. Mrs. A. M. R. (Case No. C-433), age 55, was operated upon May 29, 1941. Her icterus index on May 26, 1941 was 55. Mr. E. B. McM. (Case No. C-244), age 64, was operated upon July 17, 1942. His icterus index on July 14, 1942, was 33, and on February 2, it was 8.

In a third case, Miss B. R. G. (Case No. B-2607), age 45, had a radical operation for cancer of the right breast on July 28, 1936. Her health seemed good until December, 1941, when she became jaundiced, without pain, and with acholic stools. On January 6, 1942, her icterus index was 131. She was operated upon January 7, 1942. No malignancy was demonstrated, but the gallbladder was enlarged, and there was slight thickening of the head of the pancreas. She had several chills during her convalescence, apparently from cholangitis. She was discharged from the hospital March 14, 1942, improved. Icterus index 28.4. Report April 1, 1942, shows some jaundice still present, and the bowels move several times a day. She has had no chills since July, 1942.

In a fourth case, following dismantling of a previous cholecystoduodenostomy, union to the gallbladder was made with sutures and entero-enterostomy of the jejunal loop with a rubber band. This case is particularly interesting, because it shows the bad result that may follow union of the gallbladder to the duodenum. If there is a benign lesion and the acid contents of the stomach are normal or elevated, sooner or later, the reflux of the gastric contents as ejected from the stomach into the duodenum and the gallbladder causes cholecystitis. Mr. L. F. (Case No. A-6273), age 44, had been operated upon elsewhere in November, 1930, for what appeared to be a benign obstruction of the terminal common duct. Cholecystostomy was performed, and the bile drained continuously onto the surface of the abdomen. On March 16, 1931, we anastomosed the gallbladder to the duodenum. He made a satisfactory immediate recovery, and for ten years seemed to be in good health. Finally, however, he had enlargement of the liver and intense jaundice. On November 4, 1941, we disconnected the cholecystoduodenostomy, closed the duodenal wound, united the gallbladder to the apex of a loop of jejunum by sutures, and made an entero-enterostomy in the limbs of the loop by a single rubber band. The liver was much enlarged and showed extensive hepatitis and cholangitis. The gallbladder was hypertrophied and thickened. Obviously, the impulse of the stomach in expelling gastric contents into the duodenum had forced the gastric contents into the gallbladder. For a while the patient did fairly well, but then he developed symptoms of sepsis and died on December 31, 1941. Necropsy showed the liver greatly enlarged, with multiple abscesses and a subdiaphragmatic abscess. The union of the bowel to the gallbladder and at the entero-enterostomy was quite satisfactory, and the communication between the limbs of the jejunum was wide, even though a single rubber band was used. This was one of the earlier cases before using the triple bands.

(1b)—*Obstruction of the Terminal Common Duct when the Gallbladder had been Previously Removed:* We have had three cases of this kind. In one, Mrs. J. F. H. (Case No. C-755), age 54, the gallbladder containing stones had been removed elsewhere about nine months before her admission to the hospital, with symptoms of common duct stone. She was jaundiced

and the liver was much enlarged. Icterus index 27. At operation, on July 18, 1941, the common duct was greatly dilated and five large stones, with some thick, muddy fluid were removed from it. A loop of jejunum was anastomosed to the common duct. A small rubber band was placed only in the jejunum and the bowel around it was sutured to the incision in the common duct with two rows of fine chromic catgut. Omentum was also sutured around the anastomosis. An entero-enterostomy was performed between the two limbs of the loop of jejunum by the single rubber band technic. The patient made a satisfactory recovery and the icterus index 18 days after operation was 8. April 3, 1943, the bile tract seems to be functioning satisfactorily.

In another case, Mrs. A. P. (Case No. A-8230) age 62, there was a fistulous tract from the common duct which seemed to discharge all of the bile externally. The gallbladder had been removed elsewhere. The fistulous tract followed along the outer wall of the duodenum. At operation, in September, 1942, a loop of jejunum was opened, sutured securely to the fistulous tract at the level of the duodenum, and a lateral anastomosis with three rubber bands was made between the two limbs of the loop of jejunum. The patient made a satisfactory recovery.

In the third case, Mrs. L. W. J. (Case No. C-3247), age 48, there was extensive pancreatitis, hepatitis and cholangitis. The diseased and thickened gallbladder had been removed by us four weeks previously. The jaundice, however, continued, and there was obstruction at the pylorus by the pancrease. Under local anesthesia, on October 20, 1942, a posterior gastro-enterostomy was performed and a loop of jejunum was anastomosed to the dilated common duct. The apex of the loop of jejunum was sutured to the undersurface of the common duct with fine chromic catgut. A rubber band was passed through the apex of the loop and the dilated common duct and was tied tightly (Fig. 7). The suturing was continued around the rubber band. This was reinforced by a few interrupted sutures of fine chromic catgut, and peritoneum-covered fat was brought around the union. An entero-enterostomy was performed between the limbs of the jejunal loop with the triple rubber band technic (Fig. 7). The icterus index which had been 100 gradually came down to 19, and the liver receded somewhat. The patient improved for a while, but then gradually sank and died January 24, 1943. Necropsy showed multiple small abscesses in the liver, one of which had ruptured. The union of the jejunum to the common duct and of the entero-enterostomy was satisfactory.

(2) —*Intestinal Obstruction:* We have had five operations of this kind in four patients. In some cases of intestinal obstruction, especially when an abdominal operation has preceded the obstruction by months or years, merely severing the obstructing adhesions is sufficient. However, in other cases there may have been organic change in the bowel from the compression, so something further is indicated. We have had two cases of this type. In one, Mr. H. C. M. (Case No. B-9798), age 47, there was complete obstruction in

the lower part of the ileum resulting from a band of adhesions that seemed to have produced some necrosis of the bowel, though there was no leakage. After dividing the band at operation on May 15, 1941, the necrotic area was protected by folding over and suturing the bowel above and below this area. However, even after dividing the band, a region of probable obstruction was left by the infolding of the bowel. The rubber band technic, using a single band in this instance (our first case), was applied and the patient made a satisfactory recovery. In intestinal obstruction where the wall of the bowel is thin, the single rubber band is probably as satisfactory as the triple rubber band, but if this had been one of the later cases, we would have used the triple rubber bands.

In another case, Mr. W. B. K. (Case No. C-2873), age 31, the patient had had his appendix removed elsewhere 14 years before being admitted to St. Elizabeth's Hospital. There had been episodes of sudden pain in the upper abdomen, which quickly disappeared. The diagnosis was uncertain. While keeping him under observation, there were several of these attacks, all with pain in the upper epigastric region. He finally had a severe continuous attack, with distension and obvious symptoms of obstruction. At operation, on October 6, 1942, a series of constricting adhesions was found extending over the lower ileum. The adhesions seemed to result from the previous appendicectomy. After dividing them the lower ileum was found to be thickened and compressed. The triple rubber band technic was used between the dilated loop of ileum just above the constriction and the cecum. The patient made a satisfactory recovery for six days, and then had symptoms of sepsis. He was operated upon again, October 12, 1942, and an abscess in the pelvis was drained. The area of the anastomosis was inspected as carefully and gently as possible, and no evidence of leakage was found. Another ileocolostomy, with rubber band, was performed just above the previous one. A Witzel-type of cecostomy was made, with a small rubber catheter. This was performed because there had developed considerable intestinal distension, apparently from the sepsis in the pelvis, rather than from mechanical obstruction as in the first instance. The catheter came out a few days later and there was no leakage of fecal matter. He recovered satisfactorily.

Another case, Miss A. C. (Case No. C-1267), age 19, had partial obstruction at the terminal duodenum. On February 12, 1942, a duodenojejunostomy was performed with a single rubber band No. 32. She made a satisfactory recovery and seemed greatly relieved.

In a fourth case, already referred to, Mrs. N. G. N. (Case No. C-2415), age 62, obstruction followed the application of the rubber bands and an open resection was performed, with recovery. There was a strangulated femoral hernia on the right side and the bowel when released showed a small bruised area. This was infolded with sutures and was by-passed with an entero-enterostomy, with the triple rubber band technic. Obstruction resulted from the combination of these procedures and a resec-

tion was performed on the 4th day after the operation. She recovered satisfactorily.

While it has been apparently proved by Gatch,[3] and others, that there is no specific toxin in intestinal obstruction and that healthy mucosa under normal conditions does not absorb the toxic material in the intestine, it is undoubtedly true that in an obstructed loop of bowel there is a great multiplication of the normal bacterial contents and the *Bacillus aerogenes capsulatus* or a similar Bacterium is usually present. An enterostomy under these conditions is by no means an innocuous procedure, even though the greatest care is taken to wall-off the bowel at the site of the operation. There is a possibility of a slight contamination following along the outer wall of the catheter or tube from the bowel into the abdominal wall. That this is not merely an academic problem has been shown in two experiences of our own. While we have performed hundreds of enterostomies with satisfactory results, in these two cases, although there had been no obvious soiling, gas infection developed in the abdominal wall and the patients died. They were given the usual treatment of free incisions, the application of peroxide of hydrogen, and roentgenotherapy.

In recent years the use of the Miller-Abbott tube has helped very much in these cases of distension, but in some cases operation must be performed, and where there is the possibility of a residual partial obstruction, an entero-enterostomy which will by-pass the lesion without opening the bowel should be an excellent procedure. This technic would seem particularly indicated where radical operation cannot be undertaken in cancer of the colon, as in the splenic flexure, though we have had no case of this kind since using the rubber bands.

(3)—*Entero-enterostomy as an Adjuvant to Anterior Gastro-enterostomy or Total Gastrectomy:* This has been undertaken three times. In the one instance of total gastrectomy the entero-enterostomy was made by a single rubber band. Mr. A. F. D. (Case No. B-8307), age 54, was operated upon March 11, 1942. He died on March 19, 1942. Necropsy showed that the patient died of pneumonia, but there was a small walled-off abscess around the junction of the jejunum with the esophagus. The entero-enterostomy with a single rubber band appeared in perfect condition. There was no leakage and practically no peritoneal reaction around it, but on opening the anastomosis the rubber band had not cut through and there was no communication.

In another case, Mrs. G. R. N. (Case No. A-35), age 64, a posterior gastro-enterostomy was performed on September 23, 1941, because there was a large obstructive mass in the pyloric region of the stomach. The posterior gastro-enterostomy did not function. An anterior gastro-enterostomy and entero-enterostomy, with a single band, were performed on October 14, 1941. This, too, did not function. Fourteen days after the anterior gastro-enterostomy, a jejunostomy was established lower down for feeding and a mushroom catheter was inserted. The patient who had

been sustained intravenously was in quite a desperate condition. The mushroom catheter pulled out because of too much tension on it where it was sutured to the skin. The patient died from peritonitis the following day. Necropsy showed no definite cause for the failure of the function of either gastro-enterostomy. The stomata were adequate and well placed. The gallbladder contained one large stone and several small ones. The gallbladder was densely adherent to surrounding tissues and to the duodenum. There had been an old perforation of the gallbladder into the duodenum, caused by the large stone, and this had been walled-off by adhesions. The mass was thought to be cancer and inoperable. The entero-enterostomy was found in good condition and 1.5 cm. in diameter. There was an error in assuming that the pyloric mass was malignant. Doubtless, if its true nature had been recognized and the proper procedure adopted, the patient would have recovered.

In a third case, Mr. W. P. M. (Case No. B-9726), age 53, was operated upon June 19, 1942. An anterior gastro-enterostomy, with entero-enterostomy by a single band, was performed for extensive infiltrating carcinoma of the stomach. He died June 30, 1942. Necropsy showed death due to pulmonary embolism. The entero-enterostomy showed a very small opening.

(4) *The Mikulicz-type of Operation:* There are four cases under this head. The triple rubber band technic may be used a short distance below the ends of the bowel (Figs. 8, 9, 10 and 11). Drawing the rubber bands tightly during insertion makes the procedure practically aseptic. No fecal matter escapes. A small stoma seems to be established in 48 hours, and it is usually unnecessary to remove the clamps on the ends of the bowel.

In one patient, Mrs. G. W. M. (Case No. B-7798), age 59, this entero-enterostomy was performed after resection of the cecum and ascending colon on July 24, 1942. The end of the ileum and the stump of the transverse colon were brought up as in a typical Mikulicz procedure. The three rubber bands were inserted, as described. The patient had a bad heart and died seven days after operation from cardiac failure. The bowels had moved normally. Necropsy showed no evidence of sepsis at any point. The clamps on the ends of the bowel were still holding, there was no fecal leakage, and there was a wide opening between the two limbs of the bowel. It seems that the ends of the bowel might have healed solely by the pressure of the clamps.

A rather stout patient, Mrs. H. K. P. (Case No. B-1821), age 45, had acute symptoms in the lower left abdomen. She was operated upon, November 2, 1942, the day following admission. A short segment of sigmoid was found swollen, with its mesosigmoid greatly thickened and edematous. On separating the adhesions of this segment from the parietal peritoneum some pus exuded. It was obvious that a diverticulum had perforated into the mesosigmoid and formed an abscess which had been temporarily walled-off by the parietal peritoneum. The segment of bowel, 9.5 cm. long, was doubly clamped and resected with the electric cautery, the

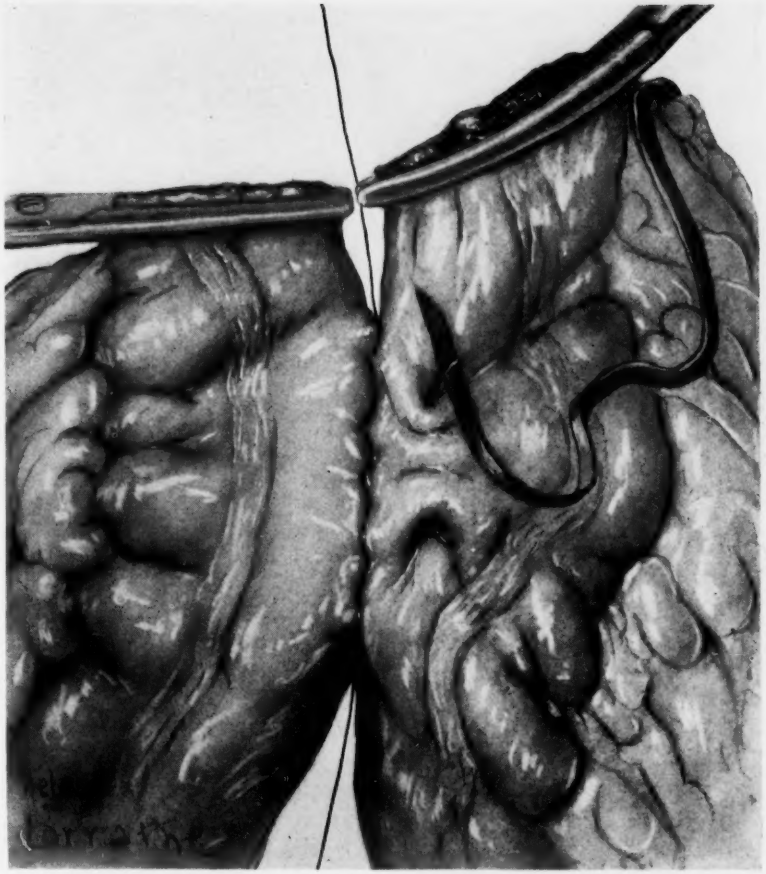

FIG. 8.—The entero-enterostomy technic is shown as applied in the Mikulicz-type of operation. A short distance from their ends the two limbs are sutured together with chromic catgut. A No. 32 rubber band is passed through first one side and then the other. Note that by puckering the bowel a large bite can be obtained.

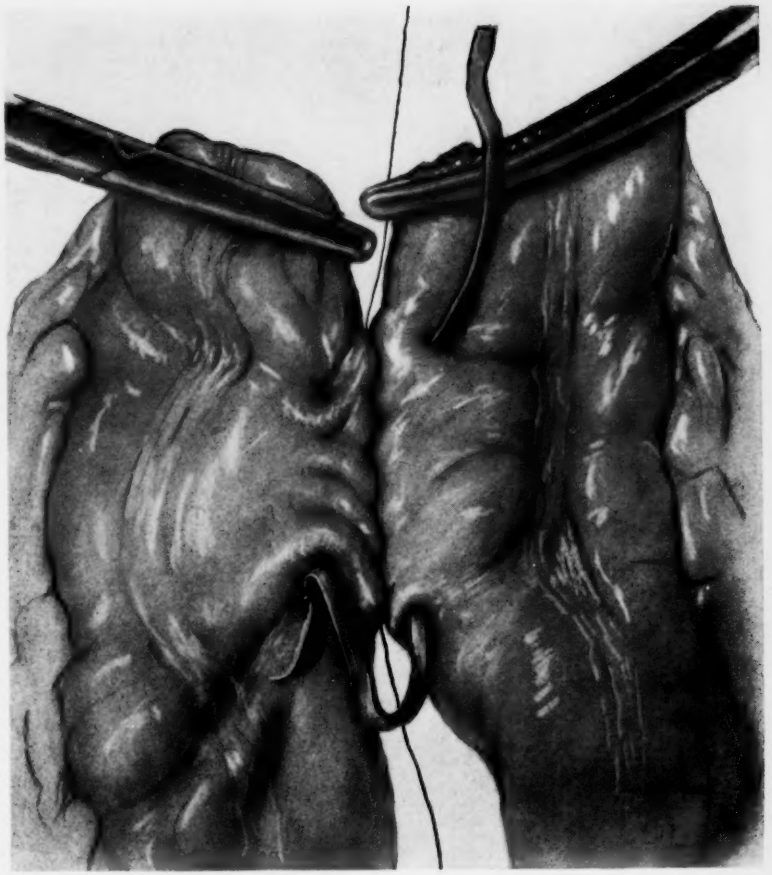

FIG. 9.—The rubber band is now passed through the left limb of the colon.

two stumps were brought into the abdominal wound as in a Mikulicz procedure, and an entero-enterostomy with the triple rubber band technic was made. The patient had very little discomfort. Seven days after operation there was a bowel movement by anus, and on the same day a small amount of fecal matter leaked from the stump of the bowel. The clamps were removed five days later (12 days after the operation). One end had apparently healed. The anastomotic opening was obstructed by an impaction of fecal matter. This was removed and, with the finger, the opening was located, and two stout rubber bands were passed through this opening

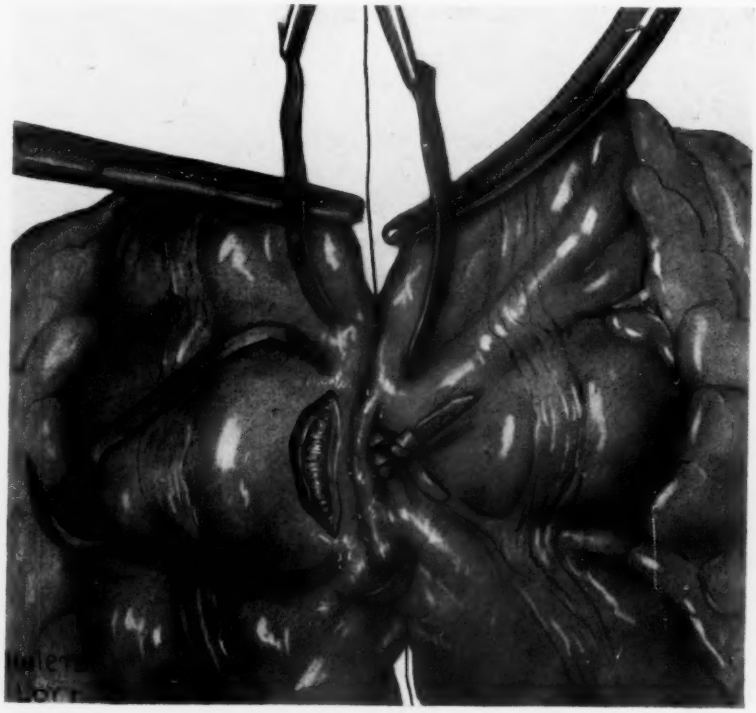

FIG. 10.—The second and third rubber bands have been passed. On the right side the second rubber band has been tied down after an incision through the peritoneum and superficial muscular coat as shown on the left side.

and tied down snugly on the remaining spur. Some sutures brought the ends of the bowel together and the abdominal wound was strapped rather snugly over them. The patient was discharged from the hospital 33 days after operation, with a small fecal fistula which would remain closed for several weeks and then would drain. On April 7, 1943, under local and sodium pentothal anesthesia, the fistula was dissected out, and the small opening in the bowel was sutured. She left the hospital the following day. The fistula had caused but little inconvenience. There was no evidence of hernia.

Mrs. G. A. J. (Case No. C-2592), age 61, entered the hospital, July 19, 1942, with intestinal obstruction from carcinoma of the splenic flexure. On the following day a cecostomy was performed. Nine days later the splenic flexure of the colon (the site of carcinoma and very adherent) was excised, including a small portion of the diaphragm. A Mikulicz operation, with the triple rubber band technic was used. On August 12th two rubber bands were passed through the entero-enterostomy opening and were tied tightly over the spur. The spur, however, continued too prominent and, August 22, 1942, three rubber bands, each on a needle, were passed through the spur, and the ends of the bowel were folded over and sutured. This was followed in a few days by rather profuse fecal discharge and the patient was losing strength, so, September 12, 1942, an attempt was made to close the colostomy. It was found that though the spur had been eliminated a portion of a loop of small bowel had been caught with a rubber band inserted on August 22, 1942, and there was a fistulous tract from the small bowel into the colon. This was disconnected, the small bowel was sutured, and the colon closed. The patient's heart condition had been poor and toward the end of the operation the blood pressure dropped and could not be restored. She died a few hours later, apparently of cardiac failure. Necropsy showed the heart about normal size, though the muscles were flabby and thin. There was infiltration around the tail of the pancreas and the diaphragm. The opening in the jejunum was about ten inches from its origin. There was no evidence of bleeding and there was practically no blood lost during the operation. The tissue from the region of the resection, however, showed cancer, which had not been removed. The presence of the fistula in the jejunum which was caused by catching a loop of the small bowel with a rubber band in a needle undoubtedly added to the weakness of the patient who was already in poor condition.

Another case, Mr. J. P. W. (Case No. C-3068), age 66, had been operated upon elsewhere about eight years before admission for carcinoma of the lower sigmoid. A resection was performed. It was a low-grade carcinoma, and he made a satisfactory recovery. Recently he developed a polypoid-like growth in the rectum. Biopsy showed low-grade cancer about grade 1.5. There was a mass in the abdomen where the resection had been previously done. There were symptoms of occasional obstruction at that point. On December 4, 1942, an abdominal incision was made. The mass consisted of infiltrated bowel at the side of the previous resection. There seemed a possibility of recurrence of the cancer, but at any rate there was obstruction at that point. A Mikulicz type of operation was performed, and the triple rubber band technic was used between the limbs of the sigmoid that were brought together. A posterior linear proctotomy was then performed, and the growth, which was on the left side of the rectum, was excised with the cautery. The segment of sigmoid was not malignant, but made an occasional obstruction. The rectal growth

was a low-grade carcinoma. On the fourth day after operation there was distension of the colon. There was apparently fecal impaction at the site of the entero-enterostomy. The proximal clamp was removed and a catheter was inserted. This relieved the symptoms. Eleven days after the operation two No. 32 rubber bands were passed through the anastomotic opening, which readily admitted the finger, and were tied down snugly on the remaining portion of the spur. A few sutures were placed on the stump of the bowel. After that there was a moderate discharge of fecal matter

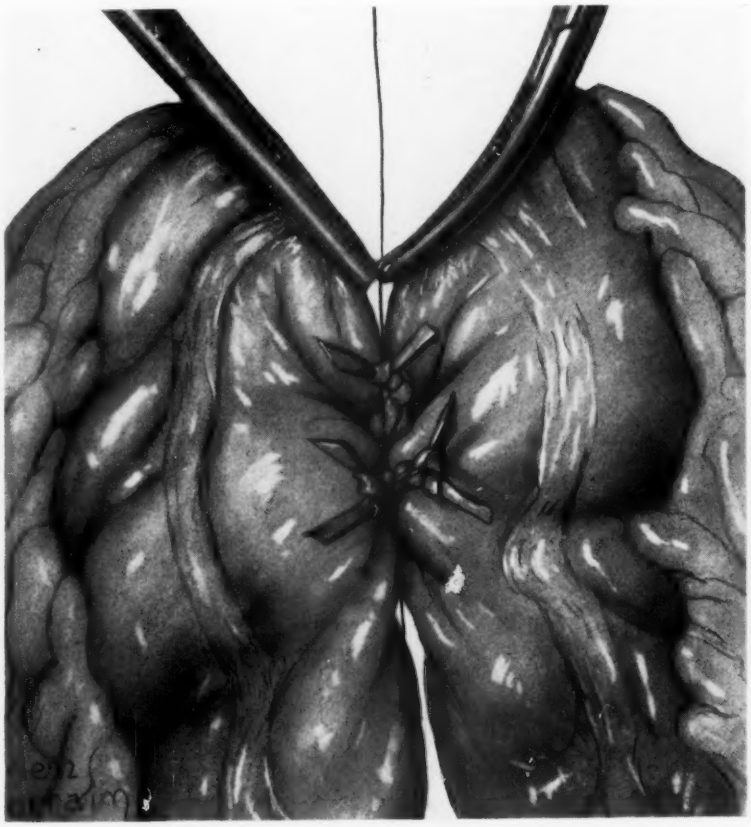

FIG. 11.—The rubber bands have all been tied and the original suture will be taken up and carried forward, burying the knots of the rubber band.

through the fistula, though the bowels moved quite freely through the rectum. However, the abdominal wall was thin and the mucosa everted. It was necessary to close the stoma on March 13, 1942. There was no recurrence of the cancer. He made a satisfactory recovery.

When the clamps are removed a rubber band may be passed down one stump, through the opening made by the rubber band entero-enterostomy, and brought up through the other stump, tied tightly, and the bowel ends

sutured over the band. This completes the division of the spur in a few days.

If the rubber band entero-enterostomy is not performed at the time of the Mikulicz operation, when the clamps are removed a few days afterward a rubber band can be passed through the spur with a needle and tied snugly (Fig. 12). The ends of the bowel are then approximated over the rubber band. There will almost certainly be some fecal leakage for a while, but it will be greatly reduced.

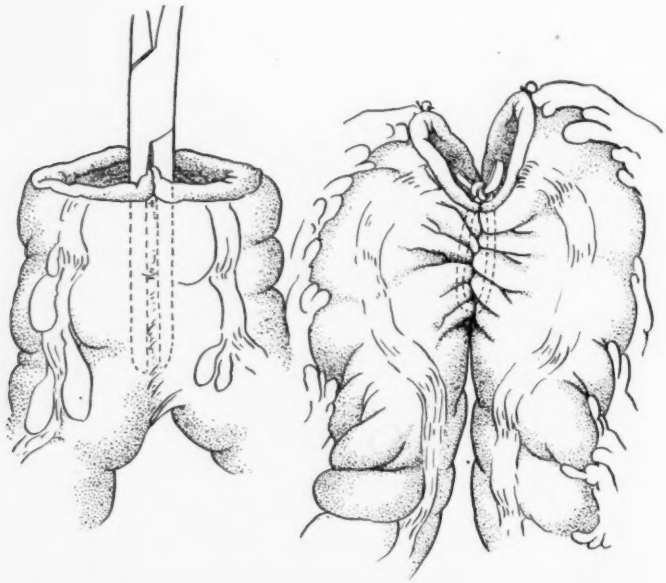

FIG. 12.—The clamps on the ends of the bowel are left on indefinitely. A communication between the two limbs of the anastomosis is doubtless established within two or three days. In one patient, Mrs. G. W. M., who died from a cardiac condition seven days after the operation, the opening was wide, there had been natural bowel movements, and the clamps were still in position with the ends of the bowel apparently healing. Usually, however, there will be some leakage from the stumps of the bowel and when the clamps are removed a rubber band can be passed through the anastomotic opening and tied down tightly on the spur, which completes the elimination of the spur, and the ends of the bowel are sutured over this. There is usually some leakage, but it may gradually cease, particularly if the abdominal wall is fat. When, however, the preliminary entero-enterostomy has not been made, a rubber band can be passed through the spur with a needle from one lumen of the stump to the other and tied down snugly. This drawing shows that such a procedure approximates the ends of the bowel much better than the application of a clamp.

SUMMARY AND CONCLUSION

A closed and practically aseptic method for cholecysto-enterostomy, choledocho-enterostomy and entero-enterostomy with ordinary rubber bands is described. No unusual apparatus or instrument is required.

When this procedure is employed in connection with the Mikulicz type of operation, it simplifies the elimination of the spur and may do away with the necessity of a subsequent formal operation for closing the bowel, which is the chief objection to the Mikulicz operation.

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SOME PHYSIOLOGIC PROBLEMS IN SURGERY OF THE PANCREAS*

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THE OPERATIONS introduced by Whipple, and his associates,[1] for the treatment of carcinoma of the ampulla, and by Brunschwig[2] for carcinoma of the head of the pancreas, result in the removal of the duodenum and portions of the pancreas varying from a small segment to seven-eighths, or more, of the entire organ. In most of the cases the pancreatic ducts are ligated so the patient is deprived of the digestive action of pancreatic juice in the intestines and the pancreas remnant undergoes varying degrees of atrophy. There are, thus, presented to the surgeon many problems that were formerly of concern only to the physiologist. I should like to comment on some of these questions and to indicate, so far as I may, the present status of our knowledge in this field.

I. IS COMPLETE REMOVAL OF THE DUODENUM COMPATIBLE WITH LIFE?

I first became interested in this problem in 1916, during the course of studies on the cause of death in intestinal obstruction.[3] At that time, it was quite generally believed that the duodenum was an organ essential to life in a manner analogous to the adrenal or parathyroid glands. The elaboration of pancreatic secretin by the duodenal mucosa had been well established, and it was thought that either this hormone was necessary or that some other similar substance indispensable to life and the function of the intestines was produced in the duodenum.[4, 5, 6]

After many unsuccessful attempts, we[7] were finally able to get a dog to survive the removal of the pyloric portion of the stomach, the entire duodenum, and the upper portion of the jejunum (Fig. 1). While the nutritive state of the animal was not good, the survival demonstrated for the first time that removal of the duodenum was permissible. It is a source of great satisfaction to me to learn from Doctor Whipple that this demonstration, among others, prompted him to undertake the operation for the radical removal of carcinoma in the ampulla of Vater in man. Subsequent experimental studies by Moorhead and Landes,[8] and Mann and Kawamura,[9] have confirmed and extended the early findings, and it is now well established that various experimental animals can survive in good health, and for long periods after complete removal of the duodenum, provided the

* The experimental studies upon which much of this paper is based were conducted with the help of associates, including F. M. Owens, Jr., J. G. Allen, D. E. Clark, O. C. Julian, and C. Vermeulen, and were aided by grants from the Josiah Macy, Jr., Foundation, the Committee on Research in Endocrinology of the National Research Council, and the Douglas Smith Foundation for Medical Research of The University of Chicago.

free flow of bile and pancreatic juice into the upper intestine is not prevented. The absence of the chief source of pancreatic secretia does not preclude, apparently, adequate pancreatic secretion. The susceptibility of these animals to the development of duodenal ulcers[9] indicates that the buffering action of the duodenal juice is, under normal conditions, of considerable importance in reducing the corrosive action of the gastric juice.

That man can also survive the complete removal of the duodenum is clear from the reports of Whipple,[10] Brunschwig,[11] and others. The data

FIG. 1.—The first mammal to survive complete duodenectomy. Operation December 15, 1917, at Iowa City, Iowa. Am. Jour. Physiol., 46, 584, 1918.

at present available, however, do not exclude the possibility that disturbances in hematopoesis, or other metabolic functions, may appear as late sequelae in man. The demonstration of the rôle of the stomach in the pathogenesis of pernicious anemia warrants the long continued study of these patients.

II. IS COMPLETE REMOVAL OF THE PANCREAS COMPATIBLE WITH LIFE?

The production of a rapidly fatal diabetes by pancreatectomy in the dog and cat, and its control by the adequate administration of insulin, is so well known that this question is better phrased as follows: Is the complete removal of the pancreas compatible with life when the ensuing diabetes is satisfactorily controlled with insulin?

At the meeting of this association in 1939, I[12] presented a summary of experimental work, conducted in our laboratory for several years, which we interpreted as follows: Confirming the previous findings of Fisher,[13] and

of Allan, Bowie, Macleod, and Robinson,[14] we reported that the depancreatized dog does not survive for long even if the diabetes is controlled by the adequate administration of insulin. At death, a majority of the animals, but not all, display a remarkable accumulation of fat in the liver. The oral administration of from 100 to 200 Gm. of raw pancreas daily suffices to prevent this fatty change in the liver and, if given along with insulin, to permit the depancreatized dog to survive for long periods, or perhaps indefinitely, in a good nutritive state. An experimental analysis led us to conclude that the beneficial effect of pancreas in this connection could not be accounted for by the presence of the pancreatic enzymes, lecithin, choline, or to the general lipotrophic action of certain proteins. It was rather due to a specific substance, not present in other organs, such as liver and brain, and the active principle was secured in fat-free, neutral, or alkaline alcohol extracts of beef or pork pancreas. This specific substance was believed to be an internal secretion of the pancreas distinct from insulin and was called "lipocaic" since it seemed to be concerned in a general way with the utilization of fat in the body.

These interpretations were not immediately accepted by all workers in this field, and a considerable effort has been made in my laboratory during the past several years to resolve the various points of conflict. Much of the difference in opinion has been due, I believe, to the fact that attention has been very largely centered on only one aspect of the problem, namely, the extensive accumulation of fat in the liver, and it has been often assumed, but without adequate proof, that the fatty livers which may be produced in normal rats by several different dietary modifications represent the same defect which appears in the insulin-treated depancreatized dog. We have repeatedly called attention to the possible error in such an assumption, and this has become more evident with the discovery that these different types of dietary fatty livers in rats do not all respond to the same kind of treatment. Fatty infiltration in the livers of normal rats may be produced by diets rich in fat, but low in protein,[15] or by the addition of thiamin to diets free from choline but rich in carbohydrates.[16] Apparently, these fatty livers may be prevented by either choline or lipocaic.[17] On the other hand, the type of fatty liver produced by the administration of liver extract or by biotin is prevented by lipocaic but not by choline.[17] Inositol is effective in preventing the biotin type of fatty liver in rats and this fact gave rise to the surmise that the active principle of lipocaic might be inositol. In recent experiments in our laboratory,[18] however, it was found that inositol was entirely ineffective in preventing or curing the fatty livers of depancreatized dogs even when used in doses as large as some of our active preparations of lipocaic. Since these pancreatic extracts could not conceivably be pure inositol it seems clear that the activity of lipocaic is not to be accounted for on the basis of the possible presence of inositol. Proof that the activity of lipocaic is not due to choline was presented in previous reports and conclusive evidence is

now available in the preparation of active pancreas extracts free from choline.[19]

These findings do not, in my estimation, lessen the significance of the work on choline. It is quite possible, for instance, that lipocaic may bear a relation to choline comparable to that existing between the parathyroid hormone and calcium. Both parathormone and calcium salts relieve the acute manifestations of parathyroid deficiency but the activity of parathormone is not due to its content of calcium. The possibility that lipocaic may play a rôle in the metabolism of fat through the agency of choline seems worthy of consideration.

McHenry[17] is reluctant to accept lipocaic as an internal secretion partly because the signs and symptoms of lipocaic deficiency do not appear for several weeks after pancreatectomy, whereas evidence of insulin deficiency becomes manifest within 24 hours. This objection seems hardly valid in view of the fact that there is a similar long latent period between removal of the thyroid or the gonads and the appearance of deficiency symptoms. The suggestion of Best, that lipocaic is not an internal secretion but rather a specific dietary factor in pancreas is perhaps a matter of definition. The relief of myxedema or cretinism by the feeding of thyroid extract could also be accounted for by the presence of a specific dietary factor in thyroid but the common view pictures this effect as due to an internal secretion.

I should like to emphasize again that we have been chiefly concerned with the deficiency which appears in the insulin treated depancreatized dog and which, unless controlled, causes death in a relatively short period of time. This deficiency is in part associated with fat metabolism as evidenced by the common appearance of fatty liver, hypolipemia, the aggravating effect of high fat diets and the beneficial action of diets low in fat. Nevertheless, it is quite possible that other and more fundamental deficiencies exist which have complicated and obscured the picture and may be in part responsible for many divergent views.

III. IS THE ATROPHY OF THE PANCREAS WHICH FOLLOWS UPON LIGATION OF THE PANCREATIC DUCTS COMPATIBLE WITH LIFE AND NORMAL NUTRITION?

In the operations for the radical removal of carcinoma of the head of the pancreas, the ampulla, or lower end of the common bile duct, the pancreatic ducts are usually ligated and remain permanently obstructed. The pancreas remnant, consisting of the tail and portions of the body, may then be expected to undergo the atrophy so well known in the experimental animal. In the early work, which demonstrated the relation of the pancreas to diabetes, it was found that successful occlusion of the pancreatic ducts in animals caused the acinar tissue to undergo almost complete degeneration and to become replaced with fibrous tissue. The islet tissue, on the other hand, persisted to a considerable extent, and the absence of diabetes in these animals provided the first evidence that it was these structures rather than the acinar tissue that was concerned in carbohydrate metabolism. With the

demonstration that lipocaic as well as insulin is required by the depancreatized dog for survival, it became important to learn if the animal with atrophy of the pancreas following duct ligation might also require lipocaic. The solution to this problem has not only immediate clinical significance but is also important in determining the source of lipocaic and its mode of production.

In one of the first papers on lipocaic from our laboratory[20] we reported that three dogs in which the ducts were successfully occluded survived for 44, 56, and 83 days, respectively, and at death extensive degeneration of the pancreas was found. A slight fatty infiltration was present in the liver of two of these animals but the third was normal. These changes were so minimal as compared with the extensive fatty infiltration usually observed after pancreatectomy that the result was considered negative. Since the acinar tissue of the pancreas had very largely disappeared, whereas the islets persisted, it was suggested that these structures were probably the source of lipocaic. In a subsequent paper[21] the *alpha* cells of the islets were suspected of being the lipocaic organ on the basis of certain indirect evidence and the solubility characteristics of the granules.

In the ensuing years a number of papers dealing with this problem have appeared, some in agreement with our early findings, others sharply divergent. We have, ourselves, continued to work in this field and the added experience has forced us to modify our interpretations somewhat. Before attempting to discuss the work of other investigators I should like to present a summary of our more recent findings. A more complete report will be published elsewhere. Successful occlusion of the pancreatic ducts has been accomplished in 19 additional dogs. These animals were fed meat, whole milk, bread, suet, cane sugar, and Brewer's yeast. Estimations of the blood lipids and sugar were made at frequent intervals, the urine was examined for sugar daily, occasional glucose tolerance tests were made, and at death a careful autopsy was performed, with microscopic examination of the liver and pancreas. The fat in the liver was determined by chemical analysis. The pancreas remnants were examined microscopically and sections, stained by Gomori's method after fixation in Bouin's fluid, were studied to determine the relative abundance of *alpha* and *beta* cells and any remaining acinar tissue.

In all of the 19 animals the pancreas was extensively atrophied at autopsy, and no ducts communicating with the duodenum were found. In ten, the liver fat was within the normal range (three to six per cent); in seven, the fat content ranged from seven to 16 per cent, and in two, the fat was in excess of 25 per cent. Fourteen survived for three months, or longer, and five over six months. Thus of a total of 22 dogs subjected to complete occlusion of the pancreatic ducts, 50 per cent displayed varying degrees of fatty infiltration of the liver, while in an equal number the livers remained normal. It is, thus, necessary for us to conclude that insofar as abnormal fat accumulation in the liver is a reliable criterion of lipocaic deficiency in this situation, a large proportion of dogs, 50 per cent in our series, develop

varying degrees of lipocaic deficiency as a result of the atrophy of the pancreas which follows successful occlusion of the pancreatic ducts.

The suggestion has been made that this fatty infiltration is due to the failure of some lipothropic substance (lipocaic) in the pancreatic juice to reach the duodenum[22] or to a digestive fault arising from the disturbance in protein digestion in the absence of the pancreatic enzymes.[17] If either of these explanations were correct one should expect as high an incidence of fatty livers after duct ligation as occurs after pancreatectomy. This is clearly not the case. In 154 insulin-treated, depancreatized dogs, reported from our laboratory several years ago,[19] 92 per cent displayed fatty infiltration in the liver attributable to lipocaic deficiency. Furthermore, the total deviation of

FIG. 2.—The photograph on the left illustrates the extensive degeneration of the pancreas three months after occlusion of the pancreatic ducts. A fibrous cord represents all that is left. The picture on the right shows the normal pancreas and adjacent duodenum.

the pancreatic juice from the intestines by means of an external fistula does not produce fatty livers. In a recent paper[23] we have reported a series of 17 animals with such fistulae, and in 15 of these the livers remained normal. This experiment appears conclusive since the juice was collected quantitatively and subsequent examination failed to reveal any abnormalities in the pancreas.

Is there another possible explanation? The view that ligation of the pancreatic ducts produces its effect solely through the removal of the pancreatic secretion has for a long time appeared to me to be not justified by the facts. The pancreas undergoes a most extensive atrophy after this procedure (Fig. 2), partly due to the pressure of accumulated secretion and partly, no doubt, to interference with the blood supply. After some months

all that remains is a thin fibrous cord. It is truly remarkable that this greatly altered organ can still perform a useful function. Microscopically, however, islet cells, identifiable as both *alpha* and *beta* types, may be discerned in a matrix of fibrous tissue and duct epithelium. Acinar cells may be entirely absent after long-standing obstruction, but usually a small number persist for several months. Such a pancreas is no longer an organ of external secretion. Is its function as an endocrine organ unimpaired? The ancient demonstration that occlusion of the ducts does not produce a diabetes comparable to that following removal of the pancreas is not particularly helpful in this connection. A surprisingly small amount of the insulin-producing tissue is adequate to prevent hyperglycemia and glycosuria. Thus, in a recent experiment we performed a partial pancreatectomy in a dog leaving a remnant of pancreas along the lesser duct. Glycosuria and hyperglycemia failed to appear, and glucose tolerance tests remained normal. The pancreas remnant weighed 2.3 Gm., and measured 1 x 1.5 x 2.5 cm. The amount of pancreas originally removed weighed 19.3 Gm., so that in this case the removal of almost nine-tenths of the original pancreas failed to produce any evidence of diabetes. The literature with respect to the influence of ligation of the pancreatic ducts on carbohydrate tolerance is conflicting, some observers reporting an increase in tolerance, others the reverse. I shall not review this data here.

Of the nineteen duct-ligated dogs in our present study, to our surprise, a moderate but definite glycosuria developed in seven. The fasting blood sugar was usually normal or somewhat lower than normal values. The ingestion of the standard diet produced a hyperglycemia ranging between 160 and 185 mg. per 100 cc., and glucose appeared in the urine. Glucose tolerance tests displayed the marked hyperglycemia and delayed return to normal characteristic of the diabetic state. There seems no doubt that these animals have become mildly diabetic. Insulin in doses of four to six units daily sufficed to control the glycosuria. When we reflect upon the relatively large proportion of the pancreas which must be removed to produce a comparable diabetes, it is evident that the islets have been extensively damaged.

In a careful study of the cytology of the pancreas of man and the dog by means of special differential stains, Gomori[24] has found both *alpha* and *delta* cells outside the islets scattered about in the acinar tissue. *Beta* cells were found only in the islets. In some dogs, Gomori[25] has estimated that the number of extra-insular *alpha* cells may actually exceed those in the islets. These observations may prove to be of great significance, for it would seem reasonable to suppose that the *alpha* cells in the acinar tissue would be even more apt to be injured by duct ligation than those in the islets. Assuming, for the moment, that the *alpha* cells are the source of lipocaic, an explanation may be seen both for the appearance of fatty livers of varying degrees in duct-ligated dogs and the marked variation in different animals in this respect. With this concept, many of the apparently contradictory findings of different observers may be harmonized. Thus, Boyce and McFetridge[26] reported that

ligation of the pancreatic ducts, with pancreas atrophy, does not cause fatty livers but when the ligation is combined with partial pancreatectomy a marked fatty infiltration occurs. In neither case does pancreatic juice reach the duodenum so the variation in result can not be accounted for on that score. It can be explained on the basis of insufficiency of islet function since we should expect this to be greater when partial pancreatectomy is added to the damage due to duct ligation. Person and Glenn[27] also observed moderate fatty infiltration of the liver in dogs subjected to duct ligation and partial pancreatectomy. The varying results obtained by other investigators may probably be accounted for depending upon the amount of injury to the islets from the accompanying fibrosis of the pancreas or to the method of duct ligation employed, some workers routinely removing the duodenal portion of the pancreas to prevent regeneration of the ducts.

Additional evidence suggesting that the *alpha* cells are the source of lipocaic has come from a different type of experiment. The repeated injection of extracts of the anterior hypophysis into dogs was found by Young[28] to produce a permanent diabetes characterized by degenerative changes in the islets. In a further study of this phenomenon, Ham and Haist[29] report that the injection of such hypophyseal extracts produced a depletion of the granules and finally hydropic degeneration of the *beta* cells. The *alpha* cells were unaffected. These dogs had severe permanent diabetes characterized by hyperglycemia, glycosuria, and a very high insulin requirement. They did not have fatty livers. These observations are of course in harmony with the view that the *beta* cells are the source of insulin. Two animals, however, were found in which the *alpha* cells were injured. "In one of these there was a complete lack of *alpha* granules and in the other a moderate degree of *alpha* cell degranulation. The islets in these animals were surrounded by acinar tissue in which the fixation and staining were excellent, hence the lack of *alpha* cell granules could not be attributed to faulty fixation or staining. These two animals, in which *alpha* cells evidenced degranulation, were the only ones in which there was an extensive deposition of fat in the liver." The authors did not interpret their experiments as indicating that the *alpha* cells are the source of lipocaic, but in a personal communication Dr. Ham informed me that this idea occurred to him. In view of the normal appearing acinar tissue it seems safe to conclude that the pancreatic secretion was unchanged and passed as usual into the duodenum. The available data thus point strongly to the conclusion that lipocaic is manufactured by the *alpha* cells of the islets and passes directly into the blood or lymph rather than into the pancreatic secretion.

Adequate data are not yet available to decide whether or no man will require lipocaic after operations which permanently obstruct the pancreatic ducts. That such procedures cause an atrophy of the pancreas resembling that which occurs in the dog is illustrated in Figure 3. In this case pancreatoduodenectomy had been performed for carcinoma of the common bile duct

and head of the pancreas. Death occurred four months later, and at autopsy the pancreatic ducts were obstructed and dilated. The islets appear to be well preserved and there was no excess fat in the liver. In one of Whipple's patients coming to necropsy nine months after occlusion of the pancreatic ducts, no fatty infiltration in the liver was found.[30] Many of the patients who have survived pancreatoduodenectomy have been given pancreatin, but since this may contain lipocaic the absence of liver fat in such cases has little significance in this problem. Brunschwig[31] occluded the pancreatic

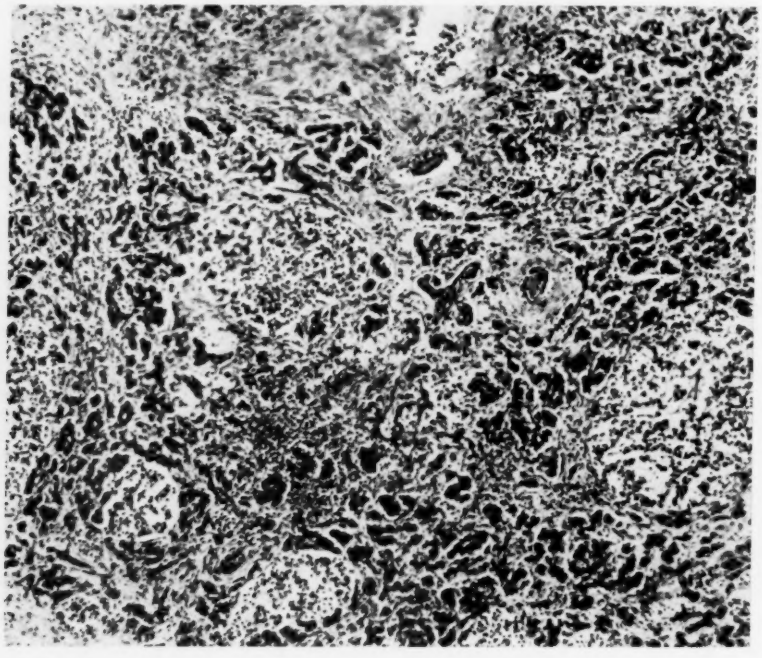

FIG. 3.—Microscopic section showing marked atrophy of the acinar tissue in human pancreas four months after resection of the head of the pancreas and permanent occlusion of the pancreatic ducts. The acinar tissue is largely, but not completely, replaced by fibrous tissue. The islets are fairly well preserved.

ducts in several monkeys and did not observe fatty livers in any case. It may be that in man and the monkey the islets are not so greatly injured by duct ligation as in the dog but until much more data become available it appears wise not to rely on such a conclusion. The greater likelihood is that a considerable proportion of these patients will develop both insulin and lipocaic deficiency in the course of time and that these sequelae will be more frequent and severe when, in addition, large portions of the pancreas are removed.

IV. WHAT EFFECTS MAY BE EXPECTED TO RESULT FROM THE COMPLETE REMOVAL OF PANCREATIC JUICE FROM THE INTESTINES?

Exclusion of pancreatic juice may be secured by total pancreatectomy, by permanent occlusion of the pancreatic ducts, or by the deviation of the

juice to the exterior by means of an appropriate fistula. Both the local and the systemic effects resulting from these procedures in experimental animals differ widely, and these should be kept in mind in a consideration of the clinical problem.

The experiments of Mann,[31] and Elman,[32] have established the fact that diversion of the pancreatic juice from the duodenum into the lower intestine, or the exterior, leads to the production of duodenal ulcers. These have been ascribed to the corrosive action of the gastric juice when its acidity has not been reduced by the sodium bicarbonate of the pancreatic secretion. In my own experience, it has been difficult to prevent the development of ulcers in dogs with total pancreatic fistulae even with the daily administration of large amounts of alkali, and I believe that ulcers would occur in almost 100 per cent if treatment were not carried out. What then is the explanation for the almost complete immunity of depancreatized dogs? In a series of over 400 such animals studied in our laboratory duodenal or gastric ulcers have been found less than a dozen times. In both cases the neutralizing effect of pancreatic juice is equally deficient yet in the one duodenal ulcer appears and in the other is absent. The animals with ligated pancreatic ducts occupy middle ground. Thirty-three per cent in our series have developed single or multiple gastric or duodenal ulcers, and several of these have perforated. Pancreatoduodenectomy in man is usually performed for the treatment of carcinoma. It is possible that a partial or complete anacidity may exist in many of these patients and for this reason ulcers may be less apt to develop than in the experimental animal. Even so, it should be remembered that an alteration in the physiology of the upper intestine conducive to the formation of ulcer has been produced and that this can be combated effectively by dietary and alkali therapy.

Although the importance of the pancreatic juice in the digestion of all three classes of foodstuffs has been recognized for many years, there is still uncertainty concerning the extent of the defect which may be expected to appear following the permanent removal of this secretion from the intestines. Most of the studies on this problem have been made upon the dog and the results here have been fairly consistent. Without exception the exclusion of pancreatic juice in this species causes the appearance of large amounts of undigested fat and protein in the feces (Pratt, Lamson and Marks,[33] Ralli, Rubin, and Present.[34] The severity of the disturbance, however, varied markedly in different animals and also in the same animal from time to time. In a recent study in our laboratory, Vermeulen and Owens[35] found that whereas the normal dog absorbed 99 per cent of neutral fat in the diet, after pancreatectomy this was reduced on an average to 47 per cent. Certain animals absorbed only 14 to 33 per cent of the fat, whereas others absorbed as much as 76 per cent. These findings confirmed the previous observations of Pratt.[36] The imperfect absorption cannot be accounted for entirely through failure of digestion of the fat since a similar, though less severe, defect was found in the absorption of fatty acids. The normal dog was found to absorb

94 per cent of oleic acid in the diet but after pancreatectomy only 63 per cent. The studies of Whipple, Bauman, and Hamlin,[37] and Brunschwig and Allen,[38] indicate that a similar disturbance in digestion and absorption, though perhaps less severe, is produced in man. Here again, marked variations were found in different patients, some displaying a very considerable defect while others were practically normal. In this connection, the remarkable ability of the pancreatic juice to find its way back into the intestines after division of the ducts should be kept in mind. This is particularly apt to occur when several anastomoses have been made. While more data on man are clearly needed, it seems probable that most patients will suffer a varying degree of impairment in the digestion and absorption of fat and protein after the operation. This is usually not so severe as to be a serious handicap and does not, of course, forbid the operation, especially since in many patients the ducts have already been obstructed by the disease. The value of substitution therapy is difficult to determine and, here again, the data on man are fortunately more favorable than in the dog. In the latter species the feeding of large amounts of fresh pancreas has been the only method in our experience that has produced a uniform and consistent improvement. Pancreas extracts containing lipocaic but no enzymes have been entirely without effect. The defect in absorption is thus apparently not due to lipocaic deficiency.

SUMMARY

The discussion of these problems has dealt almost exclusively with data obtained from the experimental animal, which in most cases has been the dog. Certain of the general conclusions derived from such work may probably be safely transferred to man, but species differences must be expected. Pancreatectomy in the monkey for instance produces a less severe diabetic state than in the dog and the same may be true of man. With this reservation in mind, the following impressions derived from work on the lower animal may be suggested as a guide in the clinical problem.

(1) Removal of from 80 to 90 per cent of the pancreas causes no defect in carbohydrate or fat metabolism or in the digestion and absorption of foodstuffs, provided the pancreas remnant remains in connection with the duct and its secretion has free access to the upper intestine.

(2) Removal of from 90 to 95 per cent of the pancreas, leaving the remnant attached to the duct, produces a diabetes, characterized by marked hyperglycemia and glycosuria, excessive insulin requirement, and hyperlipemia. Digestion and absorption are unimpaired. Lipocaic is usually required.

(3) Complete pancreatectomy produces, paradoxically, a less severe diabetes, but which is more difficult to control. Hyperglycemia and glycosuria are not so marked and less insulin is required. Hypolipemia develops and lipocaic is almost always needed. Moderate to severe impairment in the digestion and absorption of fat and protein may be expected. The absorption of carbohydrate is little affected.

(4) Permanent occlusion of the pancreatic ducts produces a similar impairment in digestion and absorption. Atrophy of the pancreas results. If partial pancreatectomy has also been performed the atrophied remnant of pancreas becomes deficient as an endocrine organ and varying degrees of lipocaic deficiency and diabetes appear. Hypolipemia becomes pronounced.

(5) Present information does not indicate that any specific defect will result from removal of the duodenum, but patients who survive for long periods after this operation has been performed should be observed carefully for the possible development of pernicious anemia.

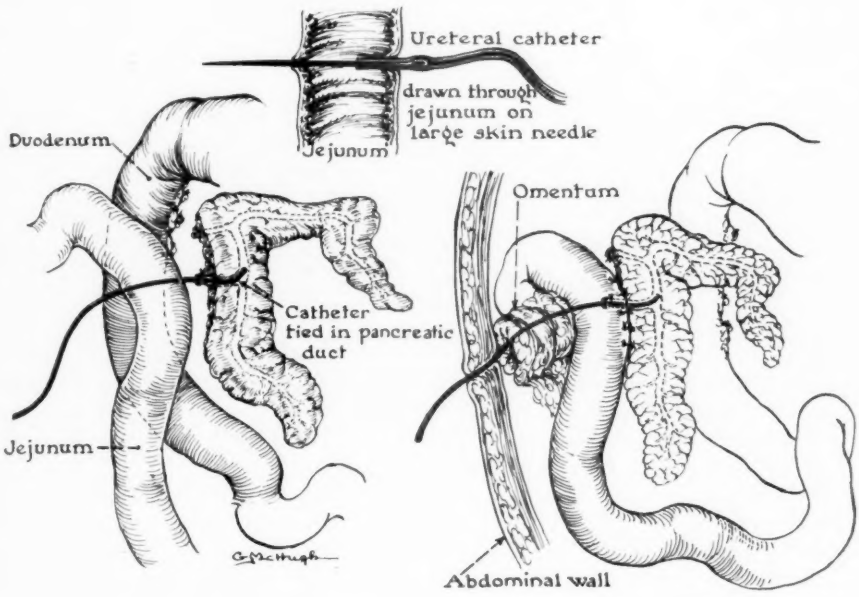

FIG. 4.—Diagrams representing a method for implanting the pancreatic duct into the jejunum which has been found successful in the dog. A ureteral catheter is introduced into the duct and ligated with fine silk. The other end of the catheter is threaded onto a spear-pointed obturator or a large skin needle. This is passed through the jejunum and traction on the catheter pulls the pancreatic duct into the jejunum. Omentum is wrapped around the catheter and jejunum and the catheter is led to the exterior by a stab wound. Pancreatic juice drains away as a fistula for five or six days. The catheter is then pulled out and the juice flows into the jejunum. The omentum prevents the formation of a jejunal fistula.

The much better nutritive state displayed by animals in which a remnant of pancreas, however small, is left in connection with its duct, as compared with those in which the ducts are occluded or the entire pancreas removed, suggests that this should be attempted whenever possible. In the treatment of carcinoma of the ampulla or head of the pancreas this will, of course, necessitate an implantation of the duct from the pancreas remnant into the stomach or intestines. Methods for accomplishing this have been devised, of which the recent one reported by Person and Glenn[27] seems especially promising. In those cases in which the duct to the remnant is dilated or readily

found, the method of implantation illustrated in Figure 4 might be tried. I have found this method satisfactory in the dog and it can be rapidly performed. This is a point of some consequence in a long and trying operation.

Substitution therapy is at present only partially effective. Pancreatin has apparently produced a definite improvement in digestion and absorption in some patients lacking pancreatic juice but in the dog fresh raw pancreas has always yielded the best results. It is probable that most preparations of pancreatin contain some lipocaic as well as the pancreatic enzymes, and in large doses might prove adequate. Preparations of lipocaic will presumably be made available by the manufacturers when sufficient published reports of its usefulness in man have appeared to satisfy the requirements of federal regulations.

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Discussion.—Dr. Allen O. Whipple (New York): Doctor Dragstedt always presents work of physiologic significance and his inquiring mind has contributed works of fundamental importance to surgery. I have followed his studies on the physiology and pathology of the pancreas with constant interest. There are certain points in his paper which I would like to discuss because of their bearings on some recent changes in our operative technic in radical pancreaticoduodenectomy.

In 22 experimental animals with duct ligation and atrophy of the acinar tissue, half of them showed no abnormal fat content of the liver and in only two was this fat content in excess of 25 per cent. This agrees with our clinical studies in humans

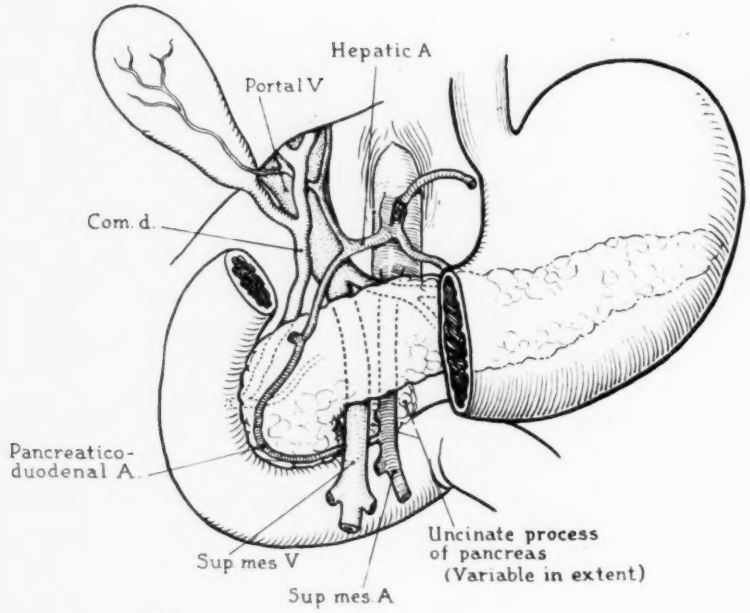
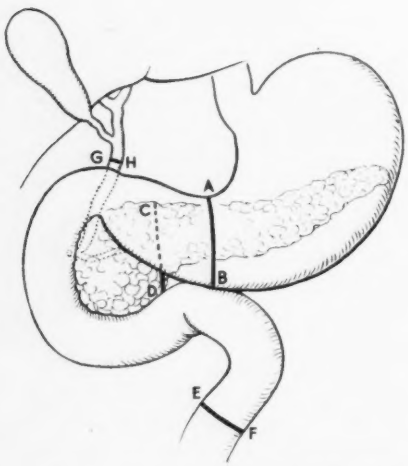


FIG. 1.—Anatomic points in pancreaticoduodenectomy. Note the importance of the variable extent of the uncinate process in its relation to the superior mesenteric vessels in removing the head of the pancreas.



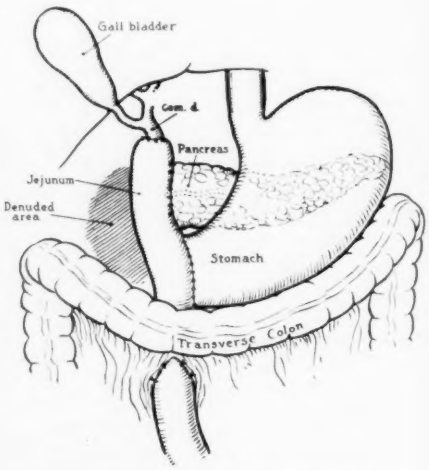


FIG. 2.—Lines of excision. A-B. Stomach. C-D. Pancreas. G-H. Common duct. E-F. Jejunum distal to duodenojejunal angle.

FIG. 3.—The one-stage operation, using the distal limb of the jejunum through the rent in the mesocolon for the anastomosis with common duct, pancreatic duct and stomach.

following pancreatic exclusion. In three patients, at intervals of two to 20 months after operation, we found that the patients digested 85 per cent of a measured fat intake. In one patient, however, without the addition of pancreatic extract in the form of haloden, she is able to digest only 40 per cent of a measured fat intake. One of the patients, with an 85 per cent fat digestion, died nine months after operation of a severe cholangitis due to stenosis of the first stage cholecystogastrostomy. The autopsy showed atrophy of the acinar tissue, persistence of islet cells, and no fatty infiltration of the liver. He had not been given any pancreas therapy.

Last week I operated upon a patient for stenosis of a posterior gastro-enterostomy which had been performed three years and eight months previously in a two-stage radical pancreaticoduodenectomy. This man has been actively engaged as a barber in one of the Army camps. After reanastomosing the stomach and jejunum I carefully examined his liver. There was no evidence of carcinoma. His liver looked normal. A biopsy of his liver tissue analyzed for fat showed only 1.9 per cent of fat. Normal rat livers yield about three per cent. His pancreas showed a fibrosis, with cystic degeneration.

The fact that in both the experimental animal and in patients having pancreas exclusion a certain number will develop impaired carbohydrate metabolism, as shown by varying degrees of a mild diabetes, points to some damage to the internal secretion mechanism both in carbohydrates and in fat metabolism. This is further indicated by the cytologic studies of Gomori, who found *alpha* and *beta* cells outside of the islets. If the *alpha* cells are the source of lipocaic, fibrosis of the excluded pancreas would cause more or less damage to or dysfunction in these *alpha* cells, and would account for the varying disturbance in fat metabolism as shown in the varying amount of fat in the liver following pancreas exclusion. The studies of Ham and Haist in diabetes produced with anterior pituitary extract, as first carried out by Young, would certainly indicate that the *alpha* cells are closely related to lipocaic production.

Because of the variable findings in both experimental animals and in man with the pancreatic juice excluded from the gastro-intestinal tract, it seemed to me that the technic of radical pancreaticoduodenectomy should be changed so as to reestablish the flow of pancreatic juice into the jejunum, in order to improve the existing impaired fat digestion of these patients in whom the flow of pancreatic juice had been blocked for varying intervals, and also to avoid the very annoying complication of a pancreatic fistula which so frequently follows the exclusion operation. The jejunum is considered preferable to the stomach because of the neutralizing effect of gastric juice on pancreatic ferments.

In the last seven of these radical operations I have reestablished the flow of pancreatic juice. In two, this has been accomplished by implantation of the pancreatic stump into the stomach, in two, by implanting the pancreatic fistula into the jejunum at a later operation, and in three I have implanted the pancreatic stump into the jejunal loop which was used for the anastomosis of the common duct and the cut end of the stomach. These two lantern slides illustrate the method of jejunal implantation carried out in the three cases in the one-stage operation. We definitely prefer the one-stage procedure and with the technic as described. This may not be the final answer, but it is a definite improvement in the evolution of the radical operation for carcinoma of the pancreas and ampullary region.

Dr. Eugene Rockey (Portland, Ore.): Last June I had the opportunity to operate upon a man who had a carcinoma of the body of the pancreas. I felt that it also involved the head of the pancreas, causing obstruction of the common duct. I, therefore, removed the lower half of the stomach, the entire pancreas, and the duodenum. The fundus of the gallbladder was anastomosed to the jejunum.

Postoperatively, we made the error of administering too much insulin in the first 24 hours, with the result that the man developed an extreme hypoglycemia and had violent convulsions. After that his diabetes was very easily controlled.

He lived 12 days, doing well, eating well, and then on the thirteenth day developed a peritonitis and died on the fifteenth day.

Death was caused by a chemical peritonitis due to a leak at the stump of the common bile duct. It would have been safer to have implanted the common bile duct into the jejunum rather than to have ligated it.

At autopsy, there was found slightly less than one Gm. of pancreatic tissue lying between the stump of the common bile duct and the hepatic artery. This patient was not given lipocaic postoperatively. Microscopic study of the liver removed at autopsy showed very little change. There were apparently some fine droplets in the cells, but they did not take a fat stain, so that there was no appreciable liver change in 15 days without pancreatic secretion.

DR. ALEXANDER BRUNSCHWIG (Chicago, Ill.): I think Doctor Dragstedt's point is well taken, that technical advances in pancreatic surgery have outstripped advances in knowledge of the physiology of this organ. We can now remove any portion of the pancreas with considerable degree of safety. Total pancreatectomies in man are possible with immediate survival from the effects of operation.

In cases where we remove large portions of the pancreas, with occlusion of the ducts, we are still unable to feel sure that indefinite survival without physiologic disturbance is possible in the face of occluded external pancreatic secretion. Some patients have survived many months without secretion of pancreatic juice into the bowel. Others present bulky fatty stools after pancreatoduodenectomy.

This variability in reaction to the occlusion of pancreatic secretion, that Doctor Dragstedt and Doctor Whipple have commented upon, I think indicates there are some very important factors that are at present unknown in connection with fat absorption and digestion in the bowel.

I present a section from the body of a pancreas in a patient from whom the head and neck of this organ have been removed, and who died five months later of carcinomatosis. Prior to operation there was steatorrhea, and after operation the stool remained bulky and light in color. It does show the persistence of acinar tissue and some proliferation of the ducts. In the animal degeneration of acinar tissue sometimes takes place much more rapidly after duct occlusion than in man.

Another section presented is from a pancreas of another patient operated upon about the same time as the first, by the one-stage resection. The stools, likewise, were fatty before and after operation. The acinar tissue is still present and easily recognizable, although fibrosis is more extensive than in the previous sections. This patient survived operation for five months, dying of carcinomatosis. In both of these patients the livers did not show excess fatty infiltration.

There is one point that might be emphasized, and that is the importance of the bile. In dealing with the pancreas, we tend to consider only pancreatic juice. I have observed another patient who presented steatorrhea (6 to 8 light frothy stools a day) for a period of six weeks before operation. At operation, the head of the pancreas was removed together with the duodenum, the lower end of the stomach, and upper two inches of the jejunum; and choledocho-enterostomy was performed. The first stool after operation was more nearly normal than any he had had for several weeks. The stool passed about ten days after operation, and all stools subsequently (patient alive and well one year) were practically normal. In this case, which is an interesting experiment, the one factor returned to the gastro-intestinal tract was bile. Pancreatic juice did not seem to be the factor affecting the character of the stool—since it was absent before (occluded by tumor) and after operation. It was the return of bile that seemed to be the important factor in return of normal stools.

In regard to survival with little pancreatic tissue, I simply want to cite an instance of a patient, who had a cystadenoma of the pancreas, which grew over the years until it apparently involved almost all the pancreas. Resection of the tumor left about one cubic centimeter of pancreatic tissue. The patient did not have diabetes because of the increased physiologic activity of the minute portion of pancreas left *in situ*. The patient remains well, two years after operation, with no physiologic disturbances and no evidence of hepatomegaly.

DR. RICHARD B. CATTELL (Boston): Two serious groups of symptoms may be associated with complete interruption of the pancreatic duct. In the first group

the symptoms, due to metabolic changes, result from the loss of pancreatic juices. In the second group, which is no less serious, the symptoms result from the local action of the pancreatic juices on the tissues with which they come in contact. In August, 1939, I performed my first radical resection of the pancreatic head, with a good immediate postoperative recovery except for an external pancreatic fistula, yet the patient died 17 days after operation from secondary hemorrhage from the fistulous tract. The complication of complete external pancreatic fistula is so serious that some such method as Doctor Whipple mentioned today is well worth while.

During the last nine months I have resected the head of the pancreas in seven patients, performing a radical pancreatoduodenectomy. I have attempted to transplant the pancreatic duct or ducts into the jejunum by a relatively simple technical procedure that not only implants the cut end of the pancreatic body but also accomplishes actual anastomosis of the main pancreatic duct. A description of this method appears in Surgical Clinics of North America, June, 1943 (Lahey Clinic Number).

When the pancreas is cut across, it is grasped by Allis forceps to control bleeding and to permit visualizaton of the cut surface. One can see the dilated or normal duct. This is ligated and before release, it is transfixed behind the ligature by a heavy silk suture. Mattress sutures then are used to close the pancreas and to stop bleeding. The loop of jejunum which is brought up for the biliary tract anastomosis is used for the "pancreatic anastomosis." The serosa and muscularis are incised for a distance equal to the width of the pancreas, leaving the mucosa intact. The posterior wall of the pancreas is sutured to the posterior border of the jejunal incision, following which the transfixion suture of the pancreatic duct is passed through the jejunal mucosa and tied down tightly as a necrosing suture. The anterior border of the pancreas then is approximated to the jejunum. The necrosing suture will cut through within 48 to 72 hours.

This method employs the principle of Coffey's third technic of ureteral transplantation, later modified by Lower and Higgins.

By this means we have been able to avoid a pancreatic fistula in some of our patients. In the last nine months I have performed radical pancreatoduodenectomy in a single stage in two patients, and in two stages in five patients, without operative mortality. One patient subsequently died, nine weeks after resection.

DR. LESTER R. DRAGSTEDT (closing): I regret that there is not time to discuss all of the many interesting physiologic problems that are raised in surgery of the pancreas, particularly with respect to the influence of pancreatic juice on the digestion and absorption of food stuffs both in man and the lower animals. In experimental work I have been very much impressed with the decidedly better nutritive state of the animal when even a small segment of pancreas is left attached to the duct, as compared with similar animals with extensive resection and in which the ducts are completely obstructed. The preservation of what little pancreas juice is secreted seems to be of great value. Furthermore, the atrophy due to ligation of the ducts is avoided. When, then, extensive resection of the pancreas in man must be undertaken, it would seem wise to implant the stump of pancreas or its duct into the gastro-intestinal tract. We have accomplished this successfully in the dog by a simple procedure that might be effective in man.

THE RECOGNITION AND MANAGEMENT OF ACUTE TRAUMA TO THE PANCREAS: WITH PARTICULAR REFERENCE TO THE USE OF THE SERUM AMYLASE TEST*

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THE PANCREAS is protected well by its deep situation within the abdominal cavity. Occasionally, however, it may be injured and, in a patient presenting signs of trauma to the upper portion of the abdomen, the possibility of such injury should be suspected. In some cases there may be no early evidence of damage to the pancreas; in others, signs from trauma to other abdominal viscera are likely to overshadow those arising from the pancreas. No particular group of symptoms or abdominal findings can be considered as diagnostic of injury to this organ. Recently, however, determination of the blood serum amylase has made it possible to recognize many such lesions (some of them only slight or moderate in extent) soon after they have occurred. This determination is made by the well standardized saccharogenic method of Somogyi, and his definition of the unit of blood serum amylase is used. During the last five years 1800 amylase determinations, including those in eight cases of trauma to the pancreas, have been made in the University of California Clinical Biochemistry Laboratory at the San Francisco Hospital. These cases illustrate trauma to the pancreas resulting from penetrating and nonpenetrating injuries to the abdomen and cases in which there was surgical trauma to the pancreas. In each instance of injury to the pancreas in which the determination was made, an elevation of the serum amylase above the maximum normal level (180 Somogyi units) was found at some time after the injury. This increase in the blood serum amylase following trauma to the pancreas probably results from leakage of the enzyme from the injured acini and ducts into the interstitial spaces, or into the peritoneal cavity, or both; thence, it is absorbed into the blood.

The case reports that follow illustrate several of the ways in which the pancreas may be injured and the consequent changes in the level of the serum amylase.

In Cases 1 and 2 the pancreas was injured by penetrating wounds of the abdomen.

CASE REPORTS

Case 1.—A male, age 37, received a stab wound in the epigastrium, the small opening just inferior to the xyphoid process penetrating into the abdomen. There

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

was no abdominal tenderness or spasm. Five hours after injury, and before operation, the blood serum amylase was 241 units (Fig. 1). Celiotomy showed a laceration of the transverse mesocolon and a laceration, about 1.5 cm. in length, into the parenchyma of the pancreas, with a large hematoma and some necrosis of fat near the head of that organ. The lacerations were repaired and the hematoma was evacuated. A soft-rubber (gutta percha) drain was placed adjacent to the wounded pancreas and brought out through a small stab wound in the right flank.

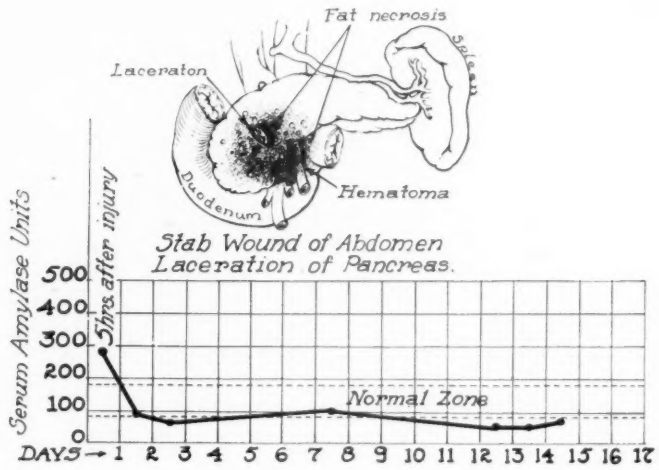

FIG. 1.—Case 1: Slight rise in serum amylase associated with a stab wound of the pancreas.

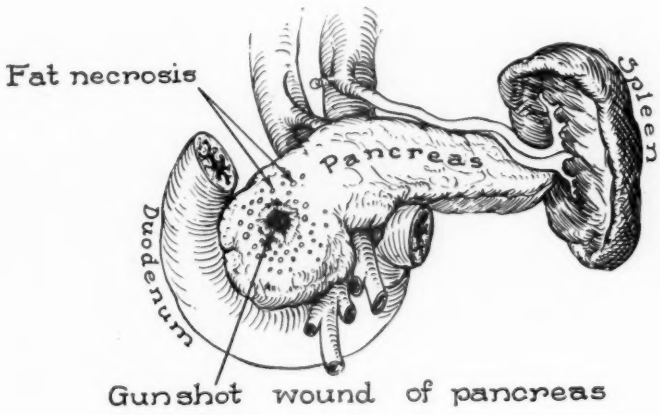

FIG. 2.—Case 2: Gunshot wound of the pancreas. The serum amylase was elevated.

Case 2.—One hour before his entry to the hospital a boy, age 12, was shot in the epigastrium with a 32-caliber pistol at a range of about 50 feet. He complained of severe abdominal pain and vomited three times. The wound of entrance was immediately beneath the costal margin about one inch to the left of the midline. The abdomen was explored through an upper left rectus incision. A considerable amount of hemorrhagic

fluid was found in the abdominal cavity, and the bullet rested between the coils of the small intestine. Perforations in the anterior and posterior walls of the stomach were closed with sutures. The lesser peritoneal cavity was soiled with gastric contents, and considerable necrosis of fat had occurred in this region. A deep wound was found in the head of the pancreas (Fig. 2). The head of the pancreas and the lesser sac were drained by cigarette drains brought out through the left rectus incision. Blood and urine amylase determinations were not made until the ninth postoperative day. A method somewhat different from that used at present was employed, but the results showed marked elevations in the amylase.

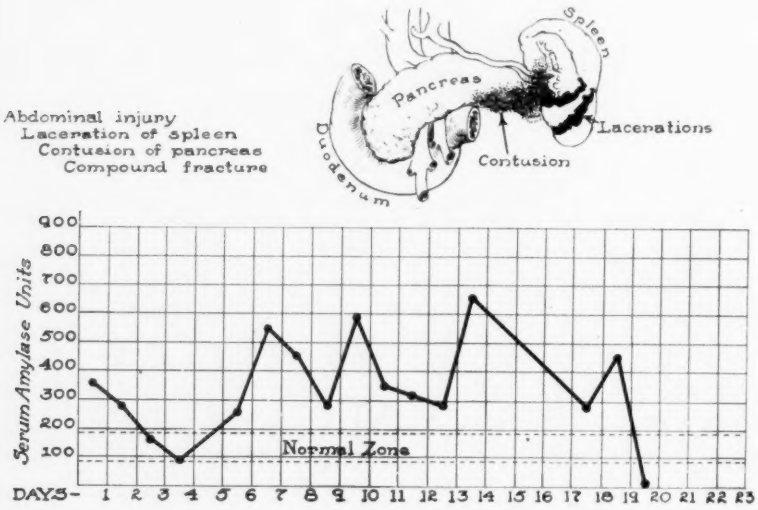

FIG. 3.—Case 3: Contusion of the pancreas following a nonpenetrating injury to the abdomen produced these elevations in the serum amylase. The readings were increased for the first two days after the injury and then subsided. On the fifth day the serum amylase again increased above normal and remained elevated for about two weeks. This probably indicated a recurrence and continuation of leakage of enzymes from the injured pancreas.

Cases 3 to 7 inclusive illustrate injuries of the pancreas resulting from nonpenetrating trauma to the abdomen.

Case 3.—A male, age 35, who had been struck by an automobile, was brought to the hospital with signs of hemorrhage, shock, a compound fracture of the leg and evidence of serious intra-abdominal injuries. The blood serum amylase was 363. After treatment for shock, the abdomen was explored through an upper left rectus incision. A large amount of blood was encountered. The spleen was lacerated extensively and the tail of the pancreas was contused and surrounded by hematoma. Splenectomy was performed and the compound fracture was débrided, reduced and immobilized. The abdomen was closed without drainage. Figure 3 shows the serum amylase studies in this case.

Case 4.—A male, age nine, was struck by an automobile about two hours before entering the hospital. There were signs of serious intra-abdominal injury with maximum findings in the upper left abdominal quadrant. Before operation the blood serum amylase was 2117 units. A lacerated spleen was removed through a left rectus incision. The abdomen contained 300 cc. of bloody fluid. The tail of the pancreas was enlarged and edematous and the surrounding area was infiltrated with blood. Two Penrose drains

were placed and brought out through a stab wound in the left flank. Figure 4 shows the serum amylase readings.*

Case 5.—A male, age 32, was injured by a severe blow in the upper portion of the abdomen. Signs indicating serious intra-abdominal injury developed while he was being observed during the subsequent eight hours. The abdomen was explored through an upper left rectus incision. Figure 5 illustrates the findings. A laceration, five centimeters in

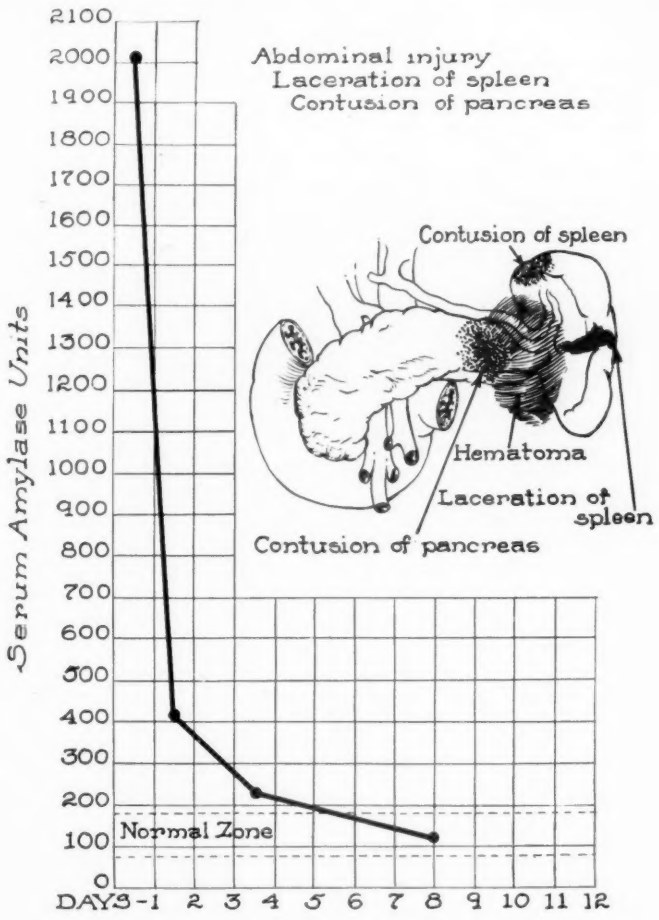

FIG. 4.—Case 4: A sharp rise and fall in the serum amylase level was associated with a contusion of the pancreas by nonpenetrating injury to the abdomen.

length, was found in the third portion of the duodenum and was closed with silk sutures. The peritoneal cavity contained bile-stained fluid and the transverse mesocolon was contused and was infiltrated with the same fluid. No determinations were made before operation, but the serum amylase was 282.5 units on the fourth postoperative day.

Case 6.—A male, age 42, was injured when the bus in which he was riding capsized. He complained of abdominal pain and signs of shock were present. There

* This case was reported in a previous article on the significance of serum amylase test in the diagnosis of acute pancreatitis.

was widespread contusion of the right upper portion of the abdominal wall. The abdomen became progressively more tender and spastic. Extensive pneumoperitoneum and subcutaneous emphysema were present. The abdomen was explored through a right upper rectus incision. The peritoneal cavity contained blood-stained bile. The first portion of the duodenum and the pyloric end of the stomach were irreparably lacerated and contused. The upper margin of the head of the pancreas was contused. Resection of the lacerated duodenum and stomach was carried out, the duodenal stump was inverted and antecolic gastrojejunostomy was performed. The serum amylase readings are shown in Figure 6.

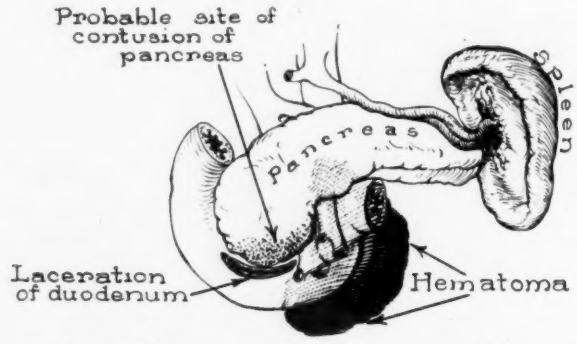

FIG. 5.—Case 5: An increase in the serum amylase was associated with laceration of the duodenum and contusion of the pancreas in this case of nonpenetrating injury of the abdomen.

Case 7.—A female, age 24, fell to the street from a height of about 60 feet. She was in a state of shock. The anterior thoracic wall was deeply contused and a fracture of the forearm and signs of serious intra-abdominal injury were present. She was treated for shock. Celiotomy showed contusion of the left kidney, multiple lacerations and contusions of the spleen and severe contusion of the terminal two inches of the tail of the pancreas (Fig. 7). Splenectomy was performed. The serum amylase before operation was 215 units. A few hours after operation it was 633 units and the following day the reading was 523 units.

The serum amylase was found to be elevated in two instances in which operation was performed upon the pancreas (Cases 8 and 9).

Case 8.—A male, age 47, complained of epigastric pain and jaundice of two months' duration. Complete obstruction of the biliary tract was present. At celiotomy, a small carcinoma of the head of the pancreas was found. The head of the pancreas with part of the body was resected, the pancreatic duct was ligated and the stump of the remaining pancreas was approximated with sutures. The area was drained. The serum amylase was 310 units following operation (Fig. 8).

Case 9.—A male, age 53, complained of vomiting and icterus, without pain, of seven weeks' duration. The biliary tract was obstructed completely. A small carcinoma of the head of the pancreas was found at operation; resection of the head and part of the body of the pancreas was performed. The stump of the enlarged pancreatic duct was ligated and the divided end of the pancreas was approximated with sutures. On the day following operation the serum amylase rose to 382 units (Fig. 9) but promptly fell again. A pancreatic fistula developed on the ninth postoperative day and, at this time, a reading of 755 units was obtained (Fig. 9).

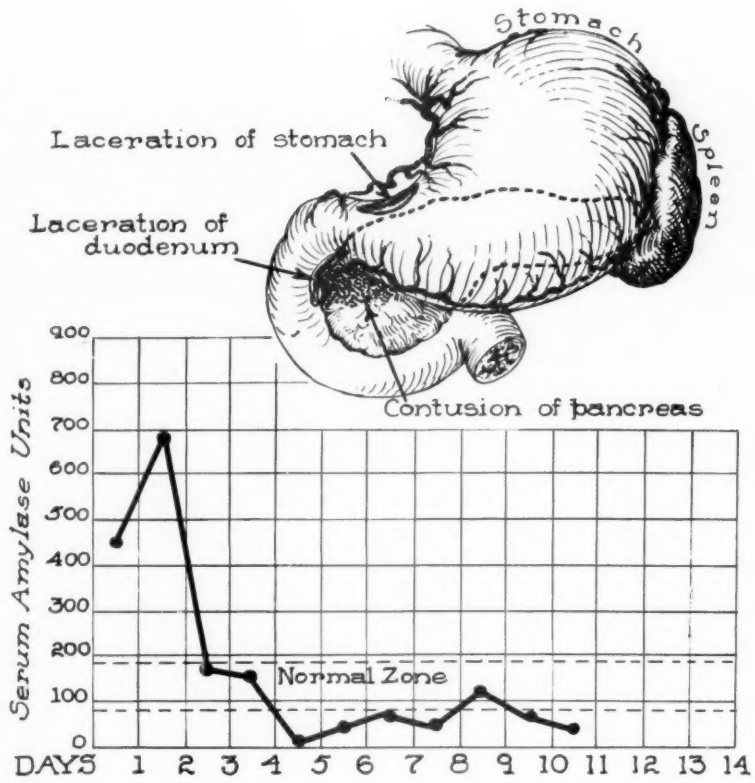

FIG. 6.—Case 6: A sharp rise and fall of serum amylase was followed by a depression of the amylase below the normal level in a case of contusion of the pancreas caused by a nonpenetrating injury of the abdomen. The duodenum and the stomach were also injured.

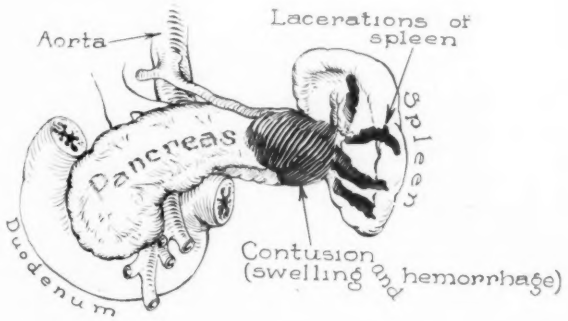

FIG. 7.—Case 7: An increase in serum amylase was associated with contusion of the tail of the pancreas. The spleen was also lacerated by this nonpenetrating injury to the abdomen.

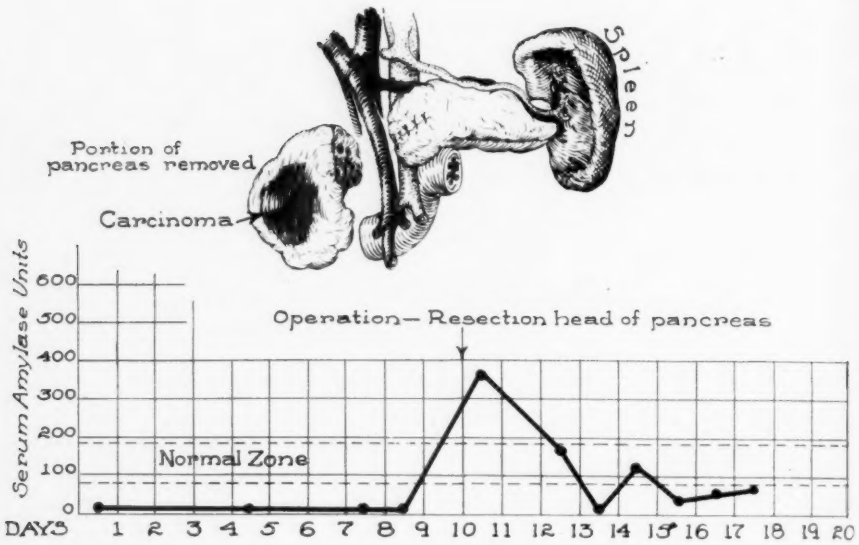

FIG. 8.—Case 8: Temporary elevation of the serum amylase followed resection of the head of the pancreas for carcinoma.

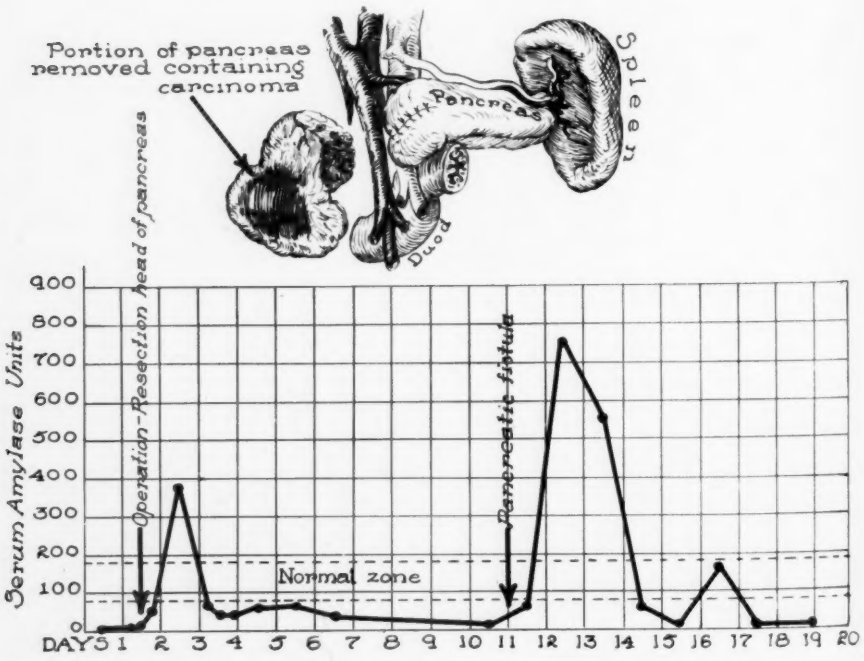

FIG. 9.—Case 9: A transient rise of serum amylase followed resection of the head of the pancreas for carcinoma. A pancreatic fistula developed on the ninth day after operation and this was associated with a secondary rise in the serum amylase.

Rarely, injury to the pancreas may occur during operations for ulcerative diseases of the stomach or duodenum when these organs must be dissected from the pancreas. Also, the pancreas may be traumatized during other difficult operations on the duodenum or lower end of the common duct. No case illustrative of this type of injury is available, however, in which a sufficient number of serial amylase determinations was done to be conclusive.

In a patient who has received an injury to the abdominal region, an elevation in the serum amylase may be considered to be good evidence that the pancreas has been damaged. In most cases there is a rapid rise and fall of the serum amylase following pancreatic injury (Figs. 1, 4 and 6), probably corresponding to the period during which enzymes leak from the injured pancreas. Obviously, it is advantageous to be able to detect evidence of trauma to the pancreas before undertaking an operation for serious injury to the abdomen. In such cases an elevated serum amylase indicates to the surgeon that the region of the pancreas should be examined carefully. When objective evidence of intra-abdominal injury is absent or uncertain, an increase in the serum amylase level occasionally may be the earliest sign of injury to the pancreas.

Lacerations of the pancreas, stab wounds and tearing injuries for example, may be closed with nonabsorbable sutures such as silk or cotton. Contused lacerations such as those received with gunshot wounds and contusions from blunt or nonpenetrating injuries usually cannot be closed. Soft rubber-tissue drains should be placed adjacent to the injured pancreas, and often these drains may be brought to the surface of the body through a small separate incision in the flank. The value of drainage in these cases is not established fully but it probably does no harm and possibly is of some efficiacy in preventing diffuse peritonitis or the formation of pancreatic pseudocyst following injury to the pancreas. In some cases pancreatic fistula forms as a result of injury to the pancreas. The skin surrounding the drains should be protected well against possible corrosive action of enzymes.

Because feeding stimulates the secretion of pancreatic juice, food should be withheld and supportive measures maintained for several days in cases in which injury to the pancreas is known or suspected. This is particularly desirable if the serum amylase level remains elevated or fluctuates, or if secondary elevations of the serum amylase occur (Figs. 3 and 9). It is probably safest to assume that such postoperative alterations in the serum amylase indicate a continuation or a recurrence of leakage of enzymes from the injured pancreas. In patients who show evidence of progressive pancreatic necrosis following injury to the pancreas, drainage of the gallbladder or common duct may be considered, but the efficacy of such a procedure has not been demonstrated. This operation was not performed in any of the cases reported here. Drugs, such as atropine, that inhibit pancreatic secretion were not given in these cases but it is possible that they might be useful.

The significance of elevations in the serum amylase occurring after oper-

ations on the pancreas, stomach, duodenum, or lower end of the common duct is probably the same as that of any other trauma to the pancreas. In such cases the principles governing the surgical and postoperative management are essentially the same as those described for cases of injury to the pancreas from external sources.

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DR. ROBERT ELMAN (St. Louis, Mo.): I would simply like to report, briefly, two observations in confirmation of those of Doctors Naffziger and McCorkle, illustrating the sensitivity and rapidity with which the serum amylase test reflects obstruction or injury to the pancreas.

The first observation was made a number of years ago, while working on pancreatic fistulae, all of the pancreatic juice flowing through a rubber tube to the outside. Many weeks after the operation, when all wounds were healed, the tube was clamped. Within *fifteen minutes* after this obstruction the serum amylase had risen from normal level to about four or five times the normal level and increased to much higher levels afterwards.

The second observation is a clinical one, details of which were furnished to me by Doctor Somogyi. A number of years ago, while studying the amylase content of a great many presumably normal serums, he ran across a specimen that contained a very high level of serum amylase. He found that this specimen was obtained shortly after an abdominal operation and that the amylase value returned to normal the next day. He was interested to know what was found at the operation. He asked the surgeon about the condition of the pancreas. The surgeon said he was sure the pancreas was quite normal because he had palpated and examined it, really vigorously, and, I am sure, massaged the whole organ from head to tail and found nothing abnormal.

TOTAL PANCREATECTOMY FOR CARCINOMA*

CASE REPORT

EUGENE W. ROCKEY, M.D.

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INTEREST in the operative removal of tumors of the pancreas has been given much greater impetus in the past fifteen years, particularly since 1935, and the number of reported cases now runs into the hundreds. A search of the literature, however, reveals only two references to so-called total pancreatectomy.

Sauve[1] says in March, 1908, concerning the case of Billroth of 1884:

"This case is mentioned in the report of Mayo-Robson at the Congress of Paris in 1901. It was probably a question of a total tumor of the pancreas, which would have necessitated total ablation of the gland; with recovery.—We have no other indications as to the operative procedure in this case; and we do not take it into consideration."

We have been unable to find any direct report of this case by Billroth.

Sauve also, in the same communication, reports Franke's case of 1900. This report quotes Franke in detail as follows:

"Woman, 68 years old, entered the Clinic on April 30, 1900. Had been operated previously on October 14, 1898, for a tumor of the pylorus, which had caused stenosis. I had done a pylorectomy with gastroduodenal anastomosis by the Kocher procedure. The results were excellent and the patient was dismissed on November 4th. The pancreas had been recognized as healthy, and besides the pyloric tumor was due to an ulcer, not a cancer.

"The patient felt very well after this first intervention until March, 1900. At this period, she became thin, lost her appetite, and noticed a tumor in the operated region. On examination, she was very thin, not recognizable, without a trace of jaundice. The scar was perfect. A little to the right of the medial line, and on this line could be felt a tumor the size of a small apple, scarcely sensitive, slightly movable transversely, much more movable from top to bottom. I thought it a recurrent carcinoma in the scar of the stomachic resection; but it was impossible to make a gastric examination, as the patient was vigorously opposed to it. She was easily persuaded to have the operation.

"*Operation:* May 1, 1900: Chloroform. Laparotomy above the umbilicus. Duration of the operation one hour and a half. Between the left lobe of the liver, the stomach and the duodenum, were thick adhesions which I had to cut with a thermocautery. The outside of the gastroduodenal anastomosis was so perfect that it almost had the look of a normal pylorus. Behind the stomach was the tumor. The head of the pancreas was invaded by the cancer, the tail appeared healthy, but on thorough examination I discovered that it showed two indurated nodules, and I decided on a total pancreatectomy. The total extirpation was difficult because the compact adhesions joined the pancreas to the retroperitoneal tissues. The adhesions were freed, partly with the thermocautery, partly with the bistoury. The ligature of the large vessels was very difficult: namely, the splenic vein had to be tied twice; numerous ligatures were placed on everything which bled. Under the head of the pancreas I found a small mass the size of a hazel-nut, situated against the duodenum. I thought that it was a question of a supernumerary pancreas, and I conserved it. After a careful drying of the peritoneum I closed the wall by layers.

"*Operative Results:* Very good. No glycosuria until the fifth day. From the fifth to the nineteenth day a moderate quantity of sugar in the urine (the maximum was 3 Gm. of sugar per litre on the eleventh day).

* Read by title before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

"The twenty-sixth day the patient left cured, without glycosuria, and eating normally. Since then, she has never had any glycosuria. Until July 30, in perfect health; from that time recurrence of the cancer with jaundice and ascites. October 16, died, five and a half months after the operation."

It is to be noted that Franke left a small mass situated against the duodenum, which he thought was possibly a supernumerary pancreas, and that the duodenum was not removed. We feel that in all likelihood a rim of the head of the pancreas adjoining the common duct was not removed, and that it was not a true total pancreatectomy. This opinion would also be substantiated by the very transitory glycosuria that developed postoperatively.

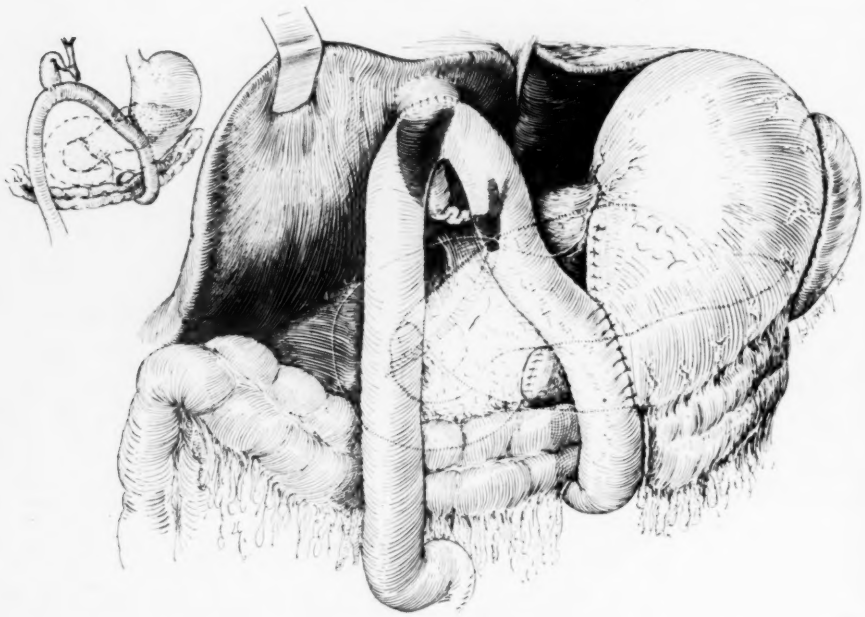

FIG. 1.—Semidiagrammatic illustration of *en bloc* total pancreatectomy, with total duodenectomy, and partial gastrectomy, with gastrojejunal and cholecystojejunal anastomosis.

Whipple[2, 3] Hunt,[4] Brunschwig,[5] Dragstedt,[6] Trimble,[7] and Harvey and Oughterson,[8] and others, have made important contributions to the technical procedures and problems met in removing the head of the pancreas and the duodenum, together with disposition of the flow.

Case Report.—A. O., male, age 51. Had been generally well until January, 1942, when he first noted abdominal pain, usually epigastric, but at times in the lower abdomen. There had been a marked weight loss. An appendicectomy had been performed elsewhere, without relief of symptoms. There was no change in bowel habit. He gave no history of jaundice. There was an increase in his abdominal distress on eating, and because of this he ate sparingly.

Physical Examination.—There was no jaundice. The heart and lungs were normal. Blood pressure 140/90. There was epigastric tenderness, but no muscle spasm. There was a well healed, lower abdominal, right rectus scar. Urine examination was negative

for sugar. Roentgenograms showed a deformity of both the pyloric end of the stomach and the duodenum. This was interpreted as due to both gastric and duodenal ulcers.

Operation.—June 19, 1942: Median epigastric incision. Exploration failed to disclose any gastric or duodenal ulcer. There was no carcinoma of the bowel. There was, however, a massive carcinoma involving chiefly the body of the pancreas. The tumor seemed to extend to the tip of the tail of the pancreas. This was rigid and about one inch in diameter. The tail was not adherent. The body of the pancreas was adherent to the aorta and to the celiac axis. The body was the size of a double fist. Some of the induration extended irregularly down into the head of the pancreas. This apparently was sufficient to cause biliary obstruction, with resultant marked dilatation of the gallbladder.

The gastrocolic omentum was divided between clamps and, in addition, the lesser curvature of the stomach was freed, giving good exposure of the growth. The gallbladder was markedly distended, and the common duct was dilated, but no stones were palpated either in the duct or gallbladder. The problem of total pancreatectomy was considered and discussed. As blood for transfusion was not available radical removal was postponed. As a palliative procedure an anastomosis was made between the fundus of the gallbladder and the anterior surface of the second portion of the duodenum. The abdominal incision was closed without drainage.

Three days later a second operation was performed. The abdomen was reopened through the upper midline incision. The cholecystoduodenostomy was taken down, and a large gauze pack placed in the right lumbar gutter. The previously made division of the gastrocolic omentum was extended in both directions. The vessels on the lesser curvature of the stomach were ligated and the stomach was divided in its midportion between Payr clamps. The entire duodenum was mobilized. The opening in the duodenum through which the cholecystoduodenostomy had been done was enlarged and retrograde catheterization of the common duct through the papilla of Vater was attempted. The papilla was found to be obstructed. The mobilized duodenum was divided just at its junction with the jejunum between clamps. The proximal end of the jejunum was closed with three layers of No. 00 chromic gut. The gastroduodenal artery was ligated and the duodenum together with the head of the pancreas was turned forward and medially. The common bile duct was clamped, cut, and ligated with chromic gut. The pancreas was freed from the superior mesenteric and the portal veins. These structures were adherent, but there was a line of cleavage. A pack was placed here. The growth apparently extended clear to the pancreatic tail. This was freed from the spleen. The pancreas was then turned forward and the pancreatic branches of the splenic artery were clamped, cut, and ligated. The tumor was not adherent to the aorta, but it was adherent to the celiac axis and to the hepatic artery. The tumor was freed from these structures with some difficulty. The entire pancreas, lower half of the stomach, and the entire duodenum were removed in one piece. An anterocolic isoperistaltic anastomosis was made between the jejunum and the open end of the stomach, with three layers of No. 00 chromic gut. An anterocolic anastomosis was then made between the jejunum, at a point eight inches distal to the gastrojejunostomy, and the previously made opening in the fundus of the gallbladder. A cigarette drain was brought out through a stab wound to the right of the main incision from the region of the stump of the ligated common duct. The incision was closed with through-and-through wires and chromic gut, silkworm gut in the skin.

The entire procedure took five hours and fifteen minutes. During the course of the operation 2200 cc. of citrated blood was administered. The patient's blood pressure and pulse rate remained the same throughout the entire operation.

Pathologic Report.—Gross: (C. H. Manlove, M.D.). "The specimen consisted of tissue from omentum, pyloric part of stomach, duodenum and pancreas. The stomach specimen consists of the pyloric and part of midgastric region. It measures 15 to 17 cm. in length from pylorus to proximal cut end. The greater curvature reveals several

lymph nodes that vary from 0.5 to 1 cm. in diameter. These nodes are firm, and when cut present compact surfaces though the larger surface appears granular. A node is present on lesser curvature near pylorus that is firm, enlarged and was removed for sectioning. The mucosa is reddened and presents usual rugated appearance, and is free from evident changes. The gastric wall shows no evident thickening.

"The duodenal tissue measures 10 cm. in length, and the pancreas is attached in usual manner. The wall of the duodenum is without apparent change. The mucosa is intact and the wall soft and pliable.

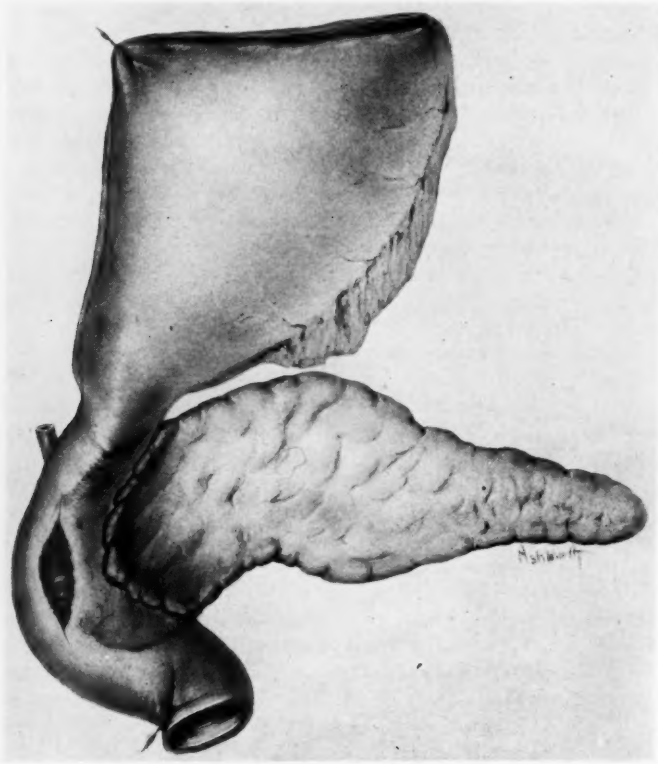

FIG. 2.—Drawing of the operatively removed specimen, the lower half of stomach, and entire duodenum and pancreas.

"The pancrease presents as an elongated rounded structure that measures 17 cm. in length. The distal 9 cm. is a dense indurated structure which, when cut, is composed of compact gray to yellow colored tissue with thin linear striations diffused throughout. Also, a duct passes through this part of the pancreas. This distal part of the pancreas appears neoplastic while the remaining proximal part presents usual soft, lobulated structural pattern of unchanged pancreas, although in the head near the duodenum, several small gray-white lobules of 2 to 3 mm. diameter are seen.

"*Histology.*—Sections through distal part of pancreas reveal much of structure composed of fibrous tissue and malignant epithelial neoplasm which replace much of the parenchyma in sections examined. The neoplasm presents as small cords, individual cells, various sized ducts and also seen involving the lining epithelium of ducts. The cells are anaplastic, hyperchromatic and tend in places to goblet cell formation. Here, in this part of the pancreas the neoplastic cells and ducts are closely invested with

fibrous tissue which varies from a dense to loose formation. At the periphery there occurs areas of gland parenchyma and within these one notes occasional compact mass of cells that may well be Langerhans' islands though no capillary channel is observed. These are noted because in other sections compact cell masses occur that suggest islands of Langerhans as isolated structures and closely invested with fibrous tissue. These are suggestive of regenerative hyperplasia of island cells. In section from midportion these islands are more frequent and in some a capillary bed is present. A large central duct passes through the section. The neoplasm approached the periphery of the section but does not appear in adjacent fat. A small lymph node is free from evidence of neoplasm. *Pathologic Diagnosis:* Adenocarcinoma of pancreas."

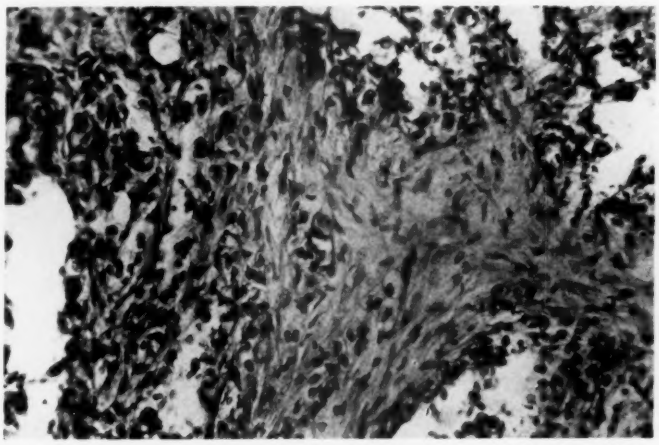

FIG. 3.—Photomicrograph illustrating the pattern of the carcinoma of the pancreas.

Postoperative Course.—The patient was in good condition upon completion of the procedure and remained so until the following day when he suffered a severe hypoglycemic reaction with violent convulsions and unconsciousness. This was relieved by administration of concentrated glucose solution. Following this the diabetes was adequately controlled. Intermittent paroxysms of hiccoughs and occasional vomiting occurred during the early postoperative period. Gastric aspiration and inhalation of carbon dioxide 10% in oxygen usually promptly relieved the patient. Fluid balance was maintained by parenteral administration.

On the 10th postoperative day bile seepage from the drainage tract was observed. It was never profuse or irritating to the skin. On the 12th postoperative day he looked well, was eating well, and said he felt well. His abdomen was soft, and his condition was good. The stools were yellow to brown in color. On the 13th postoperative day the patient complained of pain in the left upper quadrant of the abdomen and in the left lower chest on respiration. The findings on physical and roentgenologic examination were those of left lower lobe collapse. On the 14th postoperative day he complained of severe abdominal pain. His abdomen became rigid. His general condition was very poor, and in spite of all supportive treatment he became progressively worse, and on the 15th postoperative day he died.

Study of the postoperative progress of this patient, as outlined in the above summary, indicates that entirely too much insulin was administered on the first day postoperative, resulting in severe and prolonged insulin shock with convulsions. Finally, the operatively produced diabetes was controlled on an average of 27 units of regular insulin daily,

TABLE I

SUMMARY OF POSTOPERATIVE COURSE WITH REFERENCE TO INSULIN DOSAGE, GLUCOSE ADMINISTRATION AND DIET

Day of Operation

Total insulin dosage—67 units
17 units before surgery
25 units 5:15 P.M.
25 units 7:00 P.M.
Blood sugar—250 mg. at 3 P.M.
Glycosuria—3 plus at 4 P.M.
Total I.V. glucose (5%)—1700 cc.

1st Postoperative Day

Total insulin dosage—93 units
Blood sugars— 72 mg. fasting
40 mg. 12 M.
40 mg. 5 P.M.
212 mg. 7:15 P.M.
} Severe and prolonged insulin reactions
Glycosuria—none in 24 hour specimen for this day.
Total I.V. glucose—2000 cc. (5%)
50 cc. (50%)—this was given in 2 injections, 25 cc. at 12:45 P.M., and 25cc. at 3:00 P.M.

2nd Postoperative Day

Total insulin dosage—12 units
Blood sugar—80 mg. fasting
Glycosuria—23 gm. in 24 hour specimen for this day.
Total I.V. glucose—2000 cc. (5%)
10 cc. (50%)
Total I.V. saline—1000 cc.

3rd to 14th Postoperative Day

Insulin dosage raised to high of 27 units
Glycosuria—0 to 24 gm. (24 hour)
Blood sugars—200 to 286 mg.
Alkali reserve—45—(14th p.o. day)
Feedings—C– P– F–
100 60 60 throughout this period.
No evidence of ketonuria at any time during postoperative period.

which is far less than would be anticipated from the experience gained in treating patients with diabetes.

The explanation of the low insulin requirement in this patient is obscure. The lesson to be learned from the experience in this case is, as far as insulin dosage is concerned, that insulin dosage should be more accurately controlled by blood sugar determinations, and that hypoglycemia should not be produced.

Postmortem Examination.—Dr. C. H. Manlove. The body was slightly icteric. The operative wound was well healed except in its upper portion. About 500 cc. of clear yellow fluid was present in the left pleural cavity. There was almost complete atelectasis of the left lower lobe. No obstructing mucus could be demonstrated.

The abdominal cavity contained a very large amount of serofibrinous, bile-stained exudate. This exudate was found between all loops of the bowel, and had produced adhesions between these loops, and between other parts of the intestine and the abdominal wall. The pyloric end of the stomach, the duodenum, and the pancreas had been removed by surgical operative procedure *in toto*. The closed end of the first portion of the jejunum was buried in the region of the ligament of Treitz. The anastomoses between the jejunum and the stomach and gallbladder were in good condition. When these structures were ballooned out with formalin no leakage occurred. The ligated end of the common duct was not identified; apparently it was open.

The former bed of the pancreas showed a moderate inflammatory reaction and some exudate and disintegrated tissue consistent with the removal of this organ and the elapsed time.

The liver weighed approximately 1400 Gm. The surfaces made by sectioning appeared very dark brown, compact, and glistening. The bile ducts were not enlarged. The portal vein was widely patent. The splenic vein was not observed.

The small and large intestine were not unusual. A small amount of fecal material was present in the colon.

The spleen was adherent to the parietes and was coated with a serofibrinous exudate. Two irregular pale brownish areas, one somewhat round, the other elongated, measuring about 4 x 3 x 2 cm., were found in the spleen. These had the appearance of infarction.

The adrenals showed no changes. The kidneys were very soft, but were otherwise not unusual. The central nervous system was not examined.

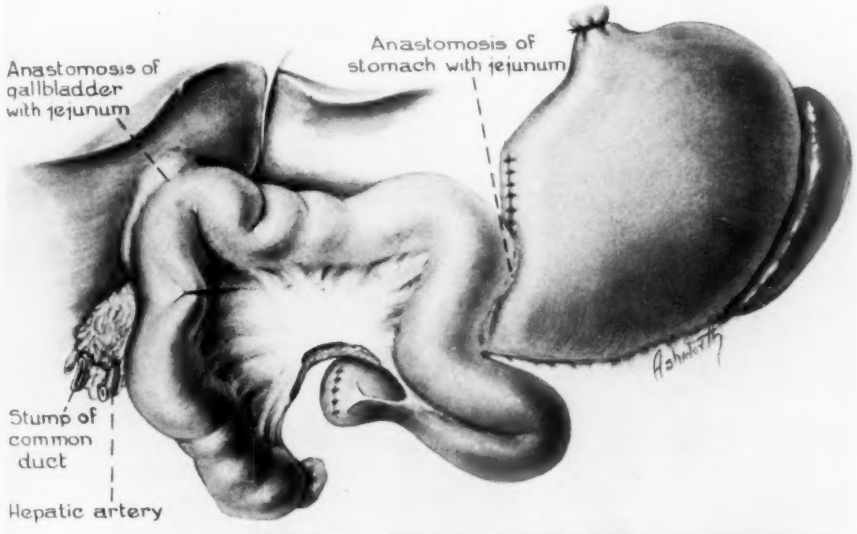

FIG. 4.—Drawing of the autopsy specimen. The hepatic artery had been divided postmortem.

Careful search and dissection of the postmortem specimen failed to disclose any residual carcinoma. There was found pancreatic tissue lying just between the stump of the common bile duct and the hepatic artery. This weighed slightly less than one Gm. (Figs. 4 and 5).

Microscopic sections of the liver reveal no striking alteration in structure that may be seen in the "hepatic trinities," or within the parenchyma itself (Fig. 6). There are no evidences of marked liver damage. Some of the liver cells appear to contain fine droplets which, however, do not stain with Sudan III. There is some dissociation in the liver cord cells which may be due to postmortem changes.

In summary, it may be pointed out that there existed a carcinoma in the distal part of the pancreas in association with distinctive fibrosis, the cause of which is not clear. If the carcinoma was superimposed upon an interstitial fibrosis and pancreatitis, it must be assumed that that had an unusual distribution, as it involved the body and tail of the pancreas without causing marked alteration in the head. It would, therefore, appear that the carcinoma and fibrous pancreatitis are included in one entity. The surgical removal of the pancreas, together with the portion of the stomach and duodenum, and the union of the gallbladder with the jejunum has not resulted in histologic evidence of liver damage or bile retention. *Cause of Death:* Carcinoma of pancreas (removed), chemical peritonitis (bile), atelectasis of lung.

Pierson[9] has recently carried on an investigation of the blood supply of the pancreas in the Department of Anatomy, University of Oregon Medical School. This comprises 50 dissections. He shows (personal communica-

FIG. 5.

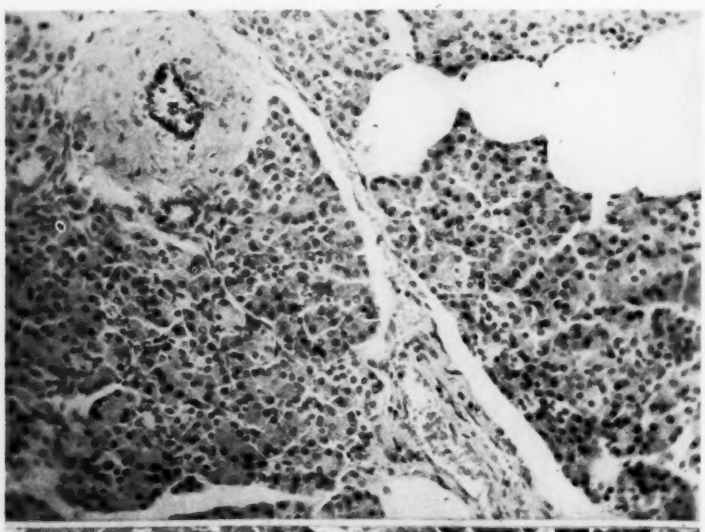

FIG. 6.

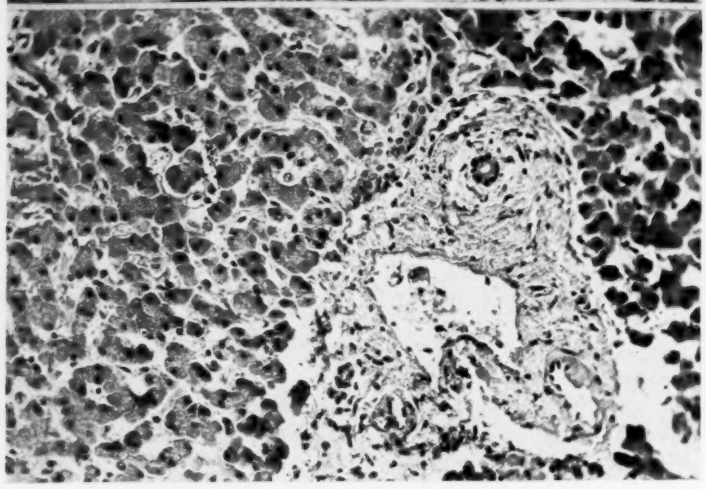

FIG. 5.—Photomicrograph illustrating the pattern of the pancreas in the small portion remaining near the ligated stump of the common bile duct. It weighed slightly less than one Gm. This pattern also prevailed in the proximal part of the operatively removed pancreas.

FIG. 6.—Photomicrograph illustrating the appearance of the apparently intact functioning liver structure, after the operation mentioned above.

tion) that as the posterior superior pancreaticoduodenal artery crosses the common bile duct it gives off small branches to it, and that these course upward from its inferior end.

COMMENT.—Had there not been the leakage of the stump of the common bile duct, and the attendant chemical peritonitis, the likelihood is that this man would have survived. The anatomic studies of Pierson show that the common bile duct usually gets its blood supply from below. As has been pointed out by both Whipple and Trimble, implantation of the common duct into the jejunum is probably a safer and wiser procedure. This would tend to give the stump of the duct additional blood supply from the jejunal host.

There were no fatty changes in the liver in the two weeks' period of time.

The insulin requirement did not reach the anticipated level. Frequent blood sugar determinations are essential to avoid hypoglycemia.

SUMMARY

A case of carcinoma of the pancreas, with total pancreatectomy has been described. Death occurred 15 days later from chemical peritonitis (bile). Suggestions for similar cases have been made.

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EXPERIMENTAL STUDIES ON PERITONEAL ADHESIONS: FOURTH REPORT—SULFONAMIDES WITH AND WITHOUT HEPARIN*

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THE PROVEN EFFECTIVENESS of the sulfonamides in controlling certain phases of infection has led to a widespread use of these drugs within the peritoneal cavity in the presence of contamination or infection.[2, 3, 4, 10, 11, 12, 13, 14] However, the literature on the relationship of the sulfonamides to the formation of peritoneal adhesions is scanty. In addition to casual references in various articles, a few specific comments may be found. For instance, Throckmorton[13] concluded from experimental work that sulfanilamide and sulfathiazole do not create adhesions in the rat. Jackson[3] found "no evidence of untoward irritation" when sulfanilamide was introduced into the normal peritoneal cavity of the dog. Corresponding in part of their respective solubilities, differing effects on tissue from local application of sulfanilamide and sulfathiazole are now recognized.[8] A clinical impression exists that similar differences occur with the use of the two drugs in the human peritoneum.[15] Part of the present study was devised to determine the relationship of sulfanilamide and sulfathiazole to the production of adhesions in the intact peritoneum of the dog.

During the past three years we have reported extensive series of experiments in the dog, demonstrating that heparin locally applied is an effective agent in the prevention of the reformation of divided intraperitoneal adhesions.[5, 6, 7] Since heparin might be indicated in the contaminated peritoneum for the prevention of adhesions, a second part of the present study was directed towards the estimation of the reformation rate of adhesions following the combined use of heparin and sulfanilamide.

METHODS

In all experiments mature mongrel dogs were used. Intraperitoneal and intravenous nembutal (Abbott) was the anesthetic agent. The skin antiseptic was Novak's solution.[9] Aseptic technic was followed throughout. Adhesions were created by scarification[7] and were divided by sharp dissection six weeks later. Hemostasis within the peritoneal cavity was effected by either silk ligature or electrocoagulation. The abdominal wall was closed in layers with silk.

The experiments consisted of three groups: (1) The effects of sulfa-

* Read by title before the American Surgical Association, Cincinnati, Ohio, May 13–14, 1943.

Aided by a grant from the John and Mary R. Markle Foundation.

thiazole and of sulfanilamide in the normal abdomen. (2) The effects of sulfathiazole and of sulfanilamide on the reformation of divided adhesions. (3) The effect of heparin combined with sulfanilamide on the reformation of divided adhesions.

The results were determined by a count of adhesions at celiotomy at least six weeks after the application of the various drugs.

The following experiments were performed:

I. *Normal Abdomen.*—A. Control: Dogs were subjected to celiotomy and the bowel and omentum were eviscerated onto warm moist towels. After the viscera were returned to the abdomen the wound was closed. B. Scarification: An attempt was made to create adhesions by extensive scarification of peritoneal surfaces. C. Dry Sulfathiazole: Upon opening the peritoneum, the bowel and omentum were delivered and laid on warm moist towels. Sterile dry sulfathiazole (Squibb) was evenly sprinkled over the bowel as it was being returned to the abdomen, the amount used being calculated on the basis of 0.5 grams per kilogram of body weight. D. Dry Sulfanilamide: Sterile dry sulfanilamide (Winthrop) was employed in the same manner and in the same dosage.

II. *Division of Adhesions—Sulfathiazole and Sulfanilamide.*—A. Dry Sulfathiazole: Adhesions were created by scarification of the peritoneum and some weeks later the abdomen was reopened. After separating the adhesions, sterile dry sulathiazole or sterile dry sulfanilamide was sprinkled evenly over the involved portions of the small bowel as it was returned to the abdomen. The dosage was again 0.5 Gm. per kilogram of body weight. B. Concentrated Sulfanilamide Solution: A saturated solution of sulfanilamide in normal saline was administered intraperitoneally by paracentesis after division of adhesions and for the first three postoperative days. One hundred and fifty cubic centimeters were given daily, either in a single dose, or divided into two doses at 12-hour intervals.

III. *Division of Adhesions—Heparin and Sulfanilamide:* A solution containing heparin* and sulfanilamide was given by paracentesis after the division of adhesions, and on three successive postoperative days. The total daily dose consisted of 150 cc. of a solution containing 1.2 Gm. of sulfanilamide (0.8 per cent) and 30 mg. (3,000 anticoagulant units) of heparin. In some experiments this amount was given once daily, and in others it was divided into two doses at 12-hour intervals.

RESULTS

I. *Normal Abdomen.*—The average number of adhesions created by the simple introduction of dry sulfathiazole was 6.3. This compares unfavorably with an average adhesion formation of 5.0 resulting from scarification of the peritoneum in 51 dogs carried out with the object of creating adhesions. With dry sulfanilamide, however, the average number of ad-

* The heparin employed was Liquaemin, furnished by the courtesy of Roche Organon, Inc.

hesions formed was only 1.6 which compares with an average of 1.1 adhesions resulting from simple celiotomy. In the sulfathiazole experiments every animal presented at least one adhesion, whereas in the sulfanilamide experiments eight animals out of fifteen presented no adhesions (Chart 1).

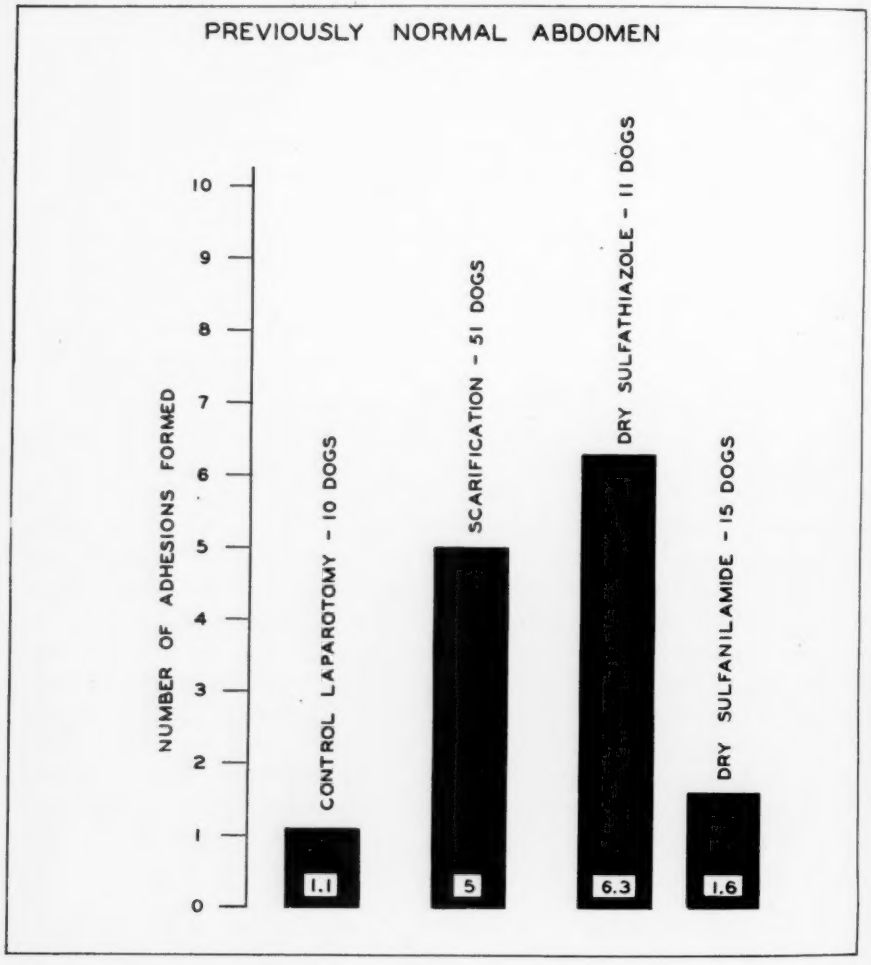

CHART 1.—Effect in the dog of dry sulfathiazole and dry sulfanilamide in the creation of adhesions in the otherwise normal abdomen.

II. *Division of Adhesions—Sulfathiazole and Sulfanilamide.*—In both groups of experiments with the dry preparation, the use of the drugs resulted in a greater number of adhesions than were divided. Following the use of sulfathiazole the average percentage of reformation was greater than 225 per cent; following the use of sulfanilamide it was greater than 175 per cent. The percentage of reformation cannot be given accurately because more adhesions were formed in nearly half the animals than could be counted.

Such animals were given a flat count of 20 adhesions, although they had more, usually many more, than that number.

With sulfanilamide solution, the results were somewhat more favorable, namely a reformation rate of only 100 per cent. There was no difference in the results between the animals given the drug once or twice daily. Both groups are, therefore, recorded together (Chart 2).

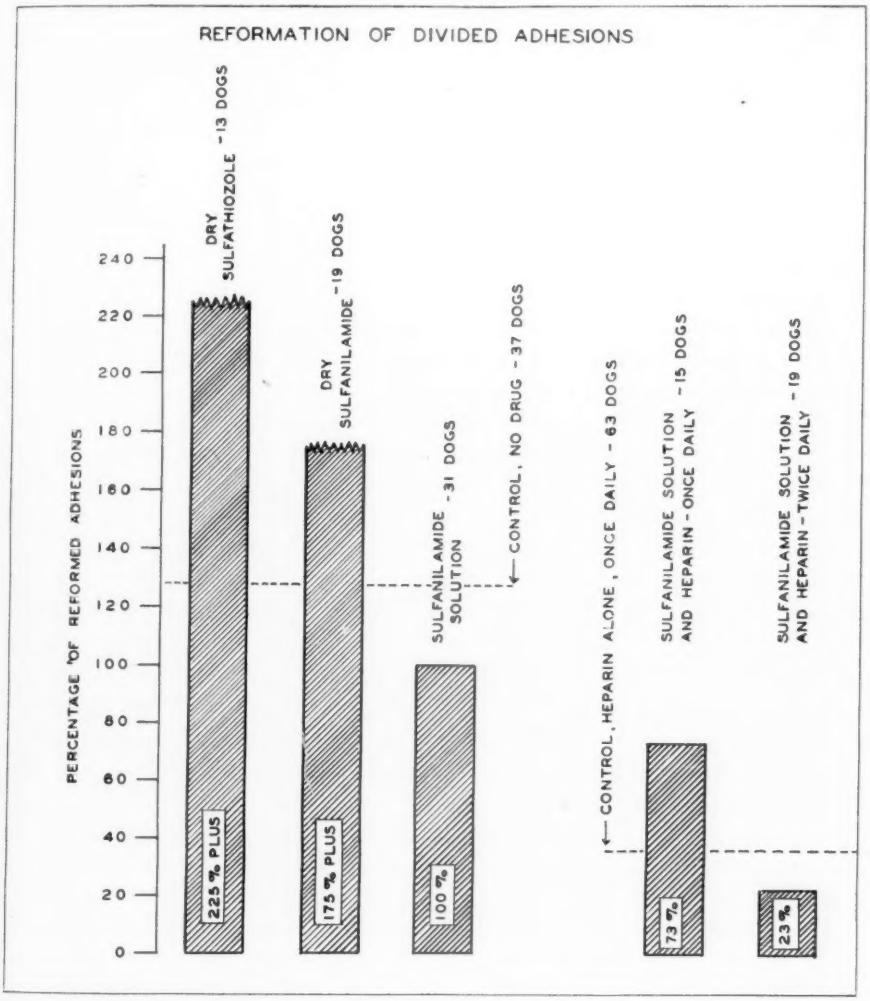

CHART 2.—Effect in the dog of dry sulfathiazole, dry sulfanilamide and sulfanilamide solution, with and without heparin, on the reformation of divided peritoneal adhesions. The broken lines at the upper limits of columns one and two indicate that the actual numbers of adhesions were greater than the heights of the columns indicate. All animals in which the numbers of adhesions were greater than 20 were counted as 20.

III. *Division of Adhesions—Heparin with Sulfanilamide.*—In these experiments there was improvement over the results with sulfanilamide alone. A striking difference was observed in the number of adhesions which reformed

depending on whether the solution was administered once or twice daily. When given once daily, the average rate of reformation was 73 per cent, and when given twice daily, it was 23 per cent.

DISCUSSION

The results of these experiments indicate a definite tendency on the part of dry sulfathiazole to create adhesions in the intact abdomen of the dog. Sulfanilamide is apparently less active. The effect of sulfathiazole is even greater than that of purposeful trauma to the peritoneum in the attempt to create adhesions, whereas the action of sulfanilamide is not significantly more harmful than the incidental trauma of simple celiotomy. The reaction to sulfathiazole may be a foreign body reaction related to the relative insolubility of the drug.

Following the division of adhesions, the deleterious effect of sulfathiazole appears to be markedly exaggerated. Curiously enough, dry sulfanilamide, although practically harmless in the intact abdomen, seemed in these experiments to be definitely active in reforming adhesions. The percentage of adhesions reformed is considerably greater than the average number reformed without the use of any drug (127 per cent), as reported in previous studies.[7] However, when sulfanilamide is exhibited in solution, even though it is readministered as often as twice a day for three successive days, the drug seems to have no great effect in modifying the reformation of adhesions. When given in this form 100 per cent of adhesions reformed.

When heparin and sulfanilamide were combined and given once daily, the results were not as good as with heparin alone, *i.e.*, 73 per cent reformation as compared with the previously reported 37 per cent reformation.[7] When, however, the same combination was given twice daily, the results improved tremendously, to an average of 23 per cent reformation. We have no figures for comparison of this last result with the use of heparin alone given twice daily. It is believed, however, that the favorable effect is due to the more continuous presence of heparin in the peritoneal cavity during the period of exudation.

In summary, these results suggest that sulfathiazole has a marked effect in tending to create adhesions in the peritoneum, and that sulfanilamide has a less harmful effect. The results of the experiments suggest, further, that from the point of view of adhesion formation sulfanilamide may be used more safely in solution than as the dry substance. What the effect of the drug in solution may be upon contamination of the peritoneum is a question not answered here. Before adopting clinically the use of the solution instead of the dry substance, experimental evidence should be available on its bacteriostatic effect in the peritoneum.

It is not believed that these experiments indicate the cessation of the current practice of using dry sulfanilamide in the peritoneum when necessary. The evidence presented, however, suggests sufficient danger of ad-

hesion formation with sulfanilamide to warrant its use in cases in which its bacteriostatic effect is urgently needed. If these experiments on the dog are applicable to the human being, the use of sulfathiazole in the peritoneum would seem to be positively contraindicated.

It must be recognized that the present experiments are conditioned by only that degree of contamination of the peritoneum which is incidental to all clean celiotomies. The effects of the drugs in the infected or contaminated peritoneum have not been examined in this study. In view of the fact that peritoneal infection is one of the commonest causes of adhesion formation, it is easy to see why both experimenters and clinical observers have gained the impression that sulfanilamide has a tendency to decrease the number of adhesions. The diminution of adhesions following peritonitis through the use of sulfanilamide might readily be predicted from the activity of sulfanilamide in controlling infection rather than from any direct virtue in the drug as an adhesion preventative.

Summary. 1. The application in the dog of dry sulfathiazole to the peritoneal surfaces in the intact abdomen and after the division of adhesions results in marked adhesion formation.

2. Dry sulfanilamide when applied to the intact peritoneal surfaces creates few adhesions. However, when applied following division of adhesions, a definite tendency towards adhesion reformation is observed. In solution, the tendency towards adhesion reformation is much less marked.

3. A solution of sulfanilamide and heparin has a slight protective effect against adhesion reformation when exhibited once daily after division of adhesions. When given twice daily, an excellent protective effect is observed.

CONCLUSIONS

1. In view of the evident tendency of sulfathiazole to create peritoneal adhesions in the dog, it should probably not be exhibited intraperitoneally in the human being.

2. Sulfanilamide in solution may offer less danger of peritoneal adhesions than the commonly used dry substance.

3. The reported experiments tend to confirm the effectiveness of heparin in preventing reformation of divided adhesions.

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CHANGES IN BRAIN VOLUME AND BLOOD CONTENT AFTER EXPERIMENTAL CONCUSSION*

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IN RECENT SURVEYS of acute craniocerebral trauma McConnell,[1] and Gurdjian, Webster, and Arnkoff[2] have reviewed the conditions which cause the brain to swell. The two basic factors concerned are intracerebral hemorrhage or congestion of the cerebral vascular tree and swelling of the cerebral tissue by extravasation of fluid into the cells or intercellular spaces. Increase in brain volume due to a single large clot or multiple petechial hemorrhages has been recorded frequently and does not require experimental confirmation. There is also the possibility of vascular congestion, which has not been thoroughly explored. While there is common agreement that localized edema occurs in an area of cerebral contusion, there is a wide divergence of opinion as to whether extravasation of fluid through the capillary walls occurs throughout the brain. Reichardt,[3] who discussed the problem of brain swelling and edema in 1927, concluded that these reactions could not be produced experimentally because of the biologic differences between animal and human brains. To date, experimental trauma has failed to produce any clear-cut proof that capillary permeability is generally increased. The most impressive investigations in this field have been made by Pilcher,[4, 5] who was unable to find any evidence in dogs of increased water content in the cerebral gray or white matter on dehydration to constant weight. In Pilcher's experiments the brain was traumatized by dropping a weight on the animal's head which was rigidly fixed in a head-holder. More recent work has shown these experiments to be open to two serious criticisms. The investigations of Denny-Brown and Russell[6] have proved conclusively that cerebral concussion does not occur when the head remains stationary. Its production requires sudden acceleration or deceleration, such as occurs when the moving head encounters an unyielding object, or the stationary head is struck by a moving one. Therefore, in Pilcher's experiments, which were made under a general anesthetic, it is most unlikely that concussion could have developed. It is unfortunate that no record of posttraumatic changes in reflexes are given in his protocols. Furthermore, Alexander and Looney,[7] in a critical survey of methods of quantitating changes in brain volume, have pointed out that the presence of cerebral edema cannot be detected with certainty by the method of dehydration. The development of improved experimental methods and the importance of a better understanding of the pathologic changes which follow intracranial injuries have led us to reopen this problem in the laboratory.

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

METHODS

Accurate methods of determining changes in volume of the brain and the blood content of the cerebral vascular tree in cats have been reported in a previous article by White, Verlot, Selverstone, and Beecher.[8] The correlation of brain volume with the capacity of the cranial chamber, originally suggested by Reichardt, was found by Alexander and Looney to be the most accurate index of variation from the normal cerebral volume in postmortem subjects. White and his coworkers adapted this procedure to cats and found it to give extremely consistent results. After decapitation and exsanguination the brain of the normal cat is from 10 to 12 per cent smaller than the surrounding cranial cavity. For convenience we shall hereafter refer to this ratio as the differential index of brain volume (D.I.B.V.). This space is occupied by the meninges and cerebrospinal fluid in the subarachnoid space, cisterns, and ventricles.

The content of blood in the cerebral tissues was determined by a method adapted by Selverstone,[8] from Bing and Baker.[9] At the moment of decapitation the neck of the animal is compressed by a powerful crushing clamp to prevent the loss of blood, and then frozen solid in dry ice. After splitting the skull and removing the frozen brain, the content of blood is determined by comparing the color reaction of hemoglobin (extracted from the macerated brain by distilled water and saponin) with benzidine against a standard prepared from a sample of the animal's own blood. The blood volume amounts to about 0.4 cc. in the brain of the normal animal, and is reduced to about half this amount after exsanguination.

Cats which were to be submitted to experimental concussion were anesthetized with nembutal (pentobarbital sodium) administered intraperitoneally (30 mg. per kilo). This dose, supplemented if necessary by additional small amounts, ensures continuous light anesthesia, with preservation of reflexes over the period of the acute experiment. In their previous investigation White, Verlot, Selverstone, and Beecher found that with this dosage of barbiturate, under normal conditions, there was no alteration in cerebral volume or blood content. When severe degrees of anoxia (arterial oxygen saturation reduced to 40 per cent) were introduced, the brain volume increased as much as 5 per cent, *viz.*, the normal differential index between brain volume and intracranial capacity was reduced from 11 to 6 per cent. While anoxia caused no congestion of the cerebral vessels, a 10 per cent rise in the carbon dioxide content of the inspired air doubled the amount of blood in the cerebral vascular tree. It was, therefore, important to prevent anoxia or hypercapnea. This was done by inserting an intratracheal cannula. In order to avoid any error, the oxygen saturation of the arterial blood and its carbon dioxide content were determined before the animals were killed.

As shown by Denny-Brown and Russell, a relatively constant degree of cerebral concussion can be produced by striking the animal a blow over the occiput with a swinging pendulum. The apparatus which we used was

designed by Professor Nathaniel H. Frank, of the Physics Department, Massachusetts Institute of Technology (Fig. 1). The striking speed of the pendulum is accelerated by heavy metal disks which are mounted eccentrically on an axle suspended on ball bearings. To obtain a slightly greater speed at impact we added a spiral spring attached to one of the disks. The striking speed of the pendulum, when released from various angles, was calculated by the number of vibrations of a tuning fork recorded on a 12-inch length of smoked paper. We did not attempt to calculate the energy produced on impact of the pendulum at various striking speeds, because its relation to concussion has been considered by Denny-Brown and Russell.

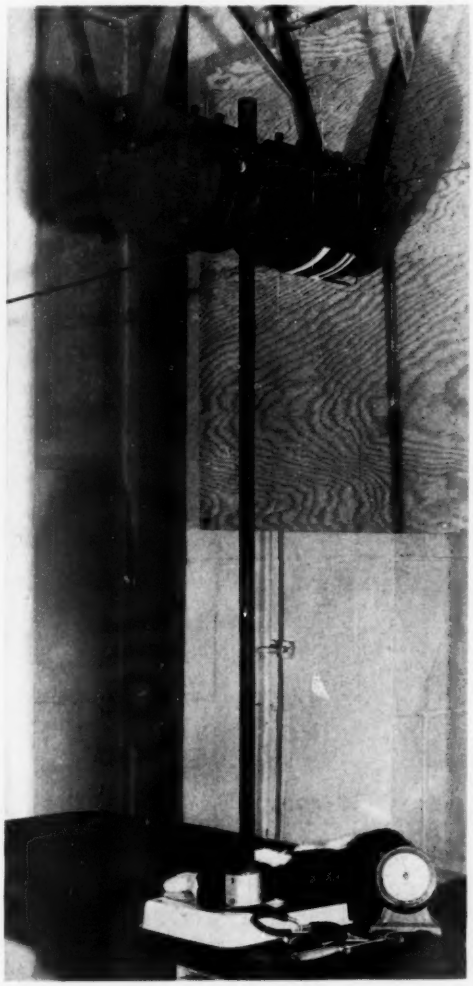

FIG. 1.—The pendulum used for producing experimental cerebral concussion. The cat is shown in position for trauma to occiput.

After the induction of anesthesia, the cat was placed on its side in position for the standard blow on the occiput. Pulse, respiration, size of pupil (in millimeters), light and corneal reflexes, and the knee jerk were recorded, the animal being observed until these observations remained constant. The pendulum was then released. Travelling at a speed up to 46.5 feet per second (31.7 miles per hour), it produces an intense blow which is sufficient to spin the animal around and throw him several feet across the table. After the trauma we repeated the above recordings of the heart and respiratory rates, size of pupils, and the reflexes at 15- to 30-second intervals until they returned to normal. A cistern puncture was then performed, and recordings of spinal fluid pressure made at regular intervals. In addition, rectal temperatures were taken and warmth applied as necessary, in order to prevent an excessive loss of body heat. At the end of varying intervals the animals were killed by decapitation with a special shears previously described.[8] This permitted

exsanguination of the head in the case of determinations of brain volume, or crushing of the neck and retention of blood in the head in cases where determinations of cerebral blood volume were to be carried out.

CEREBRAL VOLUME CHANGES AFTER CONCUSSION

A total of 24 cats have been used in these experiments. Of these, one was not traumatized, and the results in three had to be discarded, because of the presence of "snuffles" in Cats Nos. 153 and 154, and because the medulla was punctured in the course of cisternal puncture in Cat No. 151. It was felt that valid deductions on the effects of trauma on cerebral volume could be drawn from the remaining 20 animals.

In the earlier studies of White, Verlot, Selverstone, and Beecher it was found that the volume of the brain in four unanesthetized cats after exsanguination was on the average 10.5 per cent less than that of the cranial cavity. As a result of further experience we feel that this differential index of brain volume should be increased slightly, as we have found variations between 9.9 and 12.1 per cent, with an average figure of 11 per cent. The administration of pentobarbital sodium intraperitoneally caused no change in the volume of the brain, provided the oxygen saturation of the blood remained at normal levels. It has also been shown that exsanguination reduces the intracerebral blood content to a very constant residual of 0.20 cc.

The degree of concussion in lightly anesthetized cats was determined by following the changes in respiration and heart rate, the size of the pupils, and the return of the corneal and light reflexes, as suggested by Denny-Brown and Russell. The severity of concussion was graded 1, 2, or 3+, depending on the physiologic disturbances after the blow. The characteristic response was a brief period of apnea and then a recovery of the normal rate and depth of respiration. The heart rate was at first usually reduced, up to a maximum of 72 per cent, but occasionally there was a slight acceleration. Irregularities in the heart beat were frequent. The corneal reflex was consistently lost, but recovered in a period of from a few seconds up to two minutes. Dilatation of the pupil and disappearance of the light reflex roughly paralleled the loss of the corneal response. In no case were the knee jerks abolished. With the exception of Cat No. 140, where respiration failed to return, the animals appeared to have fully recovered within a period of two to four minutes. When Cats Nos. 147 to 152 (inclusive) were allowed to come out of the anesthesia, they showed no evidence of any ill effects from the concussion.

We found that pendulum-striking speeds of less than 30 feet per second failed to produce consistent evidence of cerebral disturbance. On the other hand, speeds of 46.5 feet per second caused pronounced reflex changes, basilar hemorrhages,* or occipital fractures in three animals. Of these, Cats Nos.

* This subdural and subarachnoid bleeding did not interfere with the measurement of brain volume, as the blood was thoroughly evacuated before the determinations were made. It may seem unfair to classify animals with basilar hemorrhages in the category of simple concussion. This is done because there was never any evidence of laceration or contusion of the brain and because the bleeding seemed to come from vessels in the upper cervical region.

TABLE I

SUMMARY OF DATA AFTER CEREBRAL CONCUSSION IN CATS

Cat. No.	Age*	Speed of Blow: Feet/ Sec.	Period of Apnea: Min.	Sec.	Change in Cardiac Rate: %	Pupillary Dilatation: Mm.	Loss of Reflexes: Corneal	Light	Concussion	Survival Period	D.I. B.V. %	Cerebral Swelling: %	Comment
131	Adult	34	1	30	+11	2 to 6	2 min.	2 min.	++	5½ hr.	7.6	3.4	No visible post-mortem change.
132	Young	34		30	−32	5 to 7	1 min.	1 min.	++	3 hr.	7.3	3.7	No visible post-mortem change.
133	Young	34	None		−19	0	few sec.	0	+	3 hr.	8.2	2.8	No visible post-mortem change.
134	Adult	43	1		−33	0	1 min.		++	26 min.	7.6	3.4	No visible post-mortem change.
135	Young	43		40	−25	5 to 10	30 sec.	45 sec.	++	3 hr.	7.4	3.6	Subgaleal clot. Blood over cerebellum.
136		43	1	30	−72	4 to 8	90 sec.	90 sec.	+++	5 hr.	5.9	5.1	Occipital suture sprung. Small subdural clot.
137	Adult	43	Few sec.		−25	0	Few sec.	Few sec.	+	3½ hr.	11.8	0	Subgaleal clot. Blood around brain stem.
138	Young	43	1		−45	3 to 8	..	3 min.	++	5 hr.	8.5	2.5	Occipital fracture with blood around brain stem.
139	Adult	46.5	1	10	−57	6 to 10	2 min.		+++	30 min.	9.4	1.6	Respiration not normal for 9 min. Blood clot under pons.
140	Adult	46.5	To death		−62	4 to 8	No recovery		+++	6 min.	9.0	2.0	Blood from ear. Clots along brain stem.
141	Adult	43	None		− 7	0	0	0	0	6 hr.	10.7	0	Clot under scalp
142	Adult	46.5		30	−30	0†	1 min.	4 min.	++	4 hr.	6.6	4.4	Bled from nose. Occipital fracture.
147	Young	43		7	− 5	2 to 8	1 min.	2 min.	++	24 hr.	5.4	5.6	No visible post-mortem change.
148	Young	45		10	+20	3 to 8	15 sec.	1 min.	+	24 hr.	7.2	3.8	Subgaleal and posterior fossa clots. Occipital suture sprung.
149		43		36	−29	1 to 5	40 sec.	45 sec.	++	30 hr.	7.1	3.9	Subgaleal bleeding and film of blood around brain stem.
150	Adult	45	1	30	+20	2 to 8	90 sec.	4 min.	++	30 hr.	7.9	3.1	Subgaleal bleeding and film of blood around brain stem.
151	Omitted from series because medulla was punctured.												
152	Adult	43		15	−29	5 to 8	1 min.	2 min.	++	78 hr.	11.6	0	No visible post-mortem change.
153													
154	Omitted from series because of "snuffles."												
155	Young	Control animal given second dose of pentobarbital sodium at 23 hrs.								24 hr.	10.7	0	No visible post-mortem change.
156	Adult	45		50	−45	4 to 10	100 sec.	50 sec.	++	3½ min.	12.1	0	Small subgaleal and posterior fossa clots.
157	Adult	45		45	−33	6 to 10	2 min.	2 min.	++	5½ min.	11.7	0	Small subgaleal clot.
158	Adult	45	1	15	−62	7 to 8	2 min.	45 sec.	++	16 min.	8.0	3.0	Small subgaleal clot.

Cats 143 to 146 (inclusive) were used for another type of experiment.
The dilated pupils returned to normal size with recovery of the light reflex.
With the exception of Cats 139 and 140, heart rate and respiration returned to normal in under 2 minutes.
* Age of animals was estimated by examination of teeth. No old or very young animals were used.
† Pupillary enlargement was masked by the fact that the pupils were dilated before concussion.

139 and 142 recovered within the usual four-minute period, but Cat No. 140 died in six minutes of respiratory failure. Out of nine cats submitted to a striking speed of 43 feet per second (just under 30 miles per hour), one showed a slight separation of the occipital sutures, and five showed hemorrhages around the brain stem and cerebellum. On the whole, striking speeds of from 43 to 45 feet per second seemed to be the most satisfactory and to give fairly consistent moderate degrees of concussion. These speeds are somewhat higher than those recorded by Denny-Brown and Russell, who found that evidence of concussion followed a striking speed of 28 feet per second.

The protocols of the 20 satisfactory animals, with varying degrees of cerebral concussion, are shown in Table I. We have deduced the volume of cerebral swelling from the shrinkage of the free space between the brain and the cranial cavity. As the brain in the normal animal or the cat under light pentobarbital sodium anesthesia is from 10 to 12 per cent smaller than the surrounding cranium,† a reduction of this differential index of brain volume from 11 to 6 per cent represents an expansion of the brain mass of 5 per cent. This figure cannot be influenced by vascular congestion, because it has been shown that the blood content of the exsanguinated brain is reduced to a very constant level,[8] and this was corroborated by microscopic examination of the benzidine-stained sections. A further theoretic cause of error could be distension of the ventricles by abnormal amounts of cerebrospinal fluid, as mentioned by Arnaud,[10] and other continental writers. In the previous studies of White, Verlot, Selverstone, and Beecher, hydrocephalus was routinely sought for, but no evidence of it was ever detected. Furthermore, it was observed that in the course of removing the brain from the skull the ventricular cavities were very nearly emptied of their fluid content. To verify this observation we have weighed the traumatized brain after its removal from the skull and then cut it transversely to open the lateral and third ventricles. After drying these caretully with bits of absorbent cotton and reweighing, we have found that the weight of the retained ventricular fluid amounted to no more than 0.15 to 0.25 Gm.

A study of the data in Table I shows that, although exactly comparable degrees of concussion were not produced by a given speed of acceleration of the animal's head, the amount of swelling of the brain corresponded very definitely with the posttraumatic changes observed. Striking speeds of 34 feet per second in three cats (Nos. 131, 132, and 133) produced a 2+ grade of concussion in two and a milder degree in the third. The greatest swelling occurred in Cat No. 132, and amounted to 3.7 per cent. In this animal the period of apnea lasted 30 seconds, and normal respiration had recovered at 45 seconds. The heart rate was reduced 32 per cent and remained irreg-

† As it is impossible to determine the volume of the brain before trauma, the only available figure for comparison is the average differential index in the normal animal. This objection is obviated to some extent by the small degree of variation observed.

ular for one minute. There was only slight dilatation of the pupils, and the corneal and light reflexes recovered in 60 seconds.

Striking speeds of 43 feet per second in nine animals failed to produce any definite signs of concussion in Cat No. 141, and only very mild concussion in Cat No. 137. Neither of these animals had swollen brains. In the four other cats observed over periods of from 26 minutes to five hours, brain swelling was definite, and varied from an increase of 2.5 per cent in cerebral volume to 5.1 per cent. In this latter animal (Cat No. 136) apnea lasted 90 seconds, and the heart rate was reduced 72 per cent. The corneal reflex was lost, the pupils remained dilated, and the light reflex disappeared for 90 seconds. This animal had a sprung occipitoparietal suture and a small clot under the brain stem. There was, however, no gross evidence of cerebral contusion. When the striking speed was stepped up to 46.5 feet per second in three animals, concussion ranged from 2 to 3+, but the increase in brain volume in the two cats which survived less than 30 minutes was slight. The reason for this is explained below. In the third animal, where there was a 2+ degree of concussion, the brain volume increased 4.4 per cent before decapitation four hours later. This animal was apneic for 30 seconds, and required 60 seconds to recover its normal respirations and corneal reflex. The heart rate was reduced 30 per cent, but returned to normal in four minutes. Postmortem examination showed a linear fracture running across the occiput, but there was no evidence of gross contusion of the brain.

A second point of interest is the time required for posttraumatic cerebral swelling to develop, reach its peak, and subside. When the brain volume was measured 3.5 to 5.5 minutes after moderately severe degrees of concussion in Cats Nos. 156 and 157, it remained within normal limits. In Cat No. 140, after a very severe concussion, which resulted in death from respiratory failure in six minutes, there was only 2 per cent increase in cerebral volume. In Cats Nos. 158 and 134, which were killed 16 minutes and 26 minutes after traumatization, and had 2+ degrees of concussion, there was an increase in cerebral volume of 3 and 3.4 per cent, respectively. In the four cats that were sacrificed at 24 to 36 hours,* the greatest degree of swelling seen in any animal (5.6 per cent) occurred in Cat No. 147, where concussion was moderate in degree (2+), and the animal killed 24 hours afterwards. This animal showed only a seven-second period of apnea, and a slight (5 per cent) decrease in heart rate, but the pupils dilated from 2 to 8 mm. and the corneal reflex was lost for one minute. On recovery from the anesthetic, it showed no signs of discomfort and no evidence of any neurologic abnormality. Cat No. 152 was allowed to survive for 78 hours, and then was found to have a normal-sized brain.

The relationship between time elapsing after trauma and cerebral swelling is shown in Figure 2. McConnell's[1] findings in human cases of closed head

* Whenever animals were permitted to recover from the anesthetic, they were reanesthetized before decapitation. A control cat (No. 155), submitted to a second dose of intraperitoneal pentobarbital sodium, was found still to have a normal-sized brain.

injury are of interest in this respect. He states that "generalized swelling or edema of the brain was found soon after the injury and during recovery. . . . It was not related to the state of consciousness. . . In this series of cases cerebral edema did not appear to increase the effects of the basic lesion of concussion or to delay recovery from concussion." This statement applies

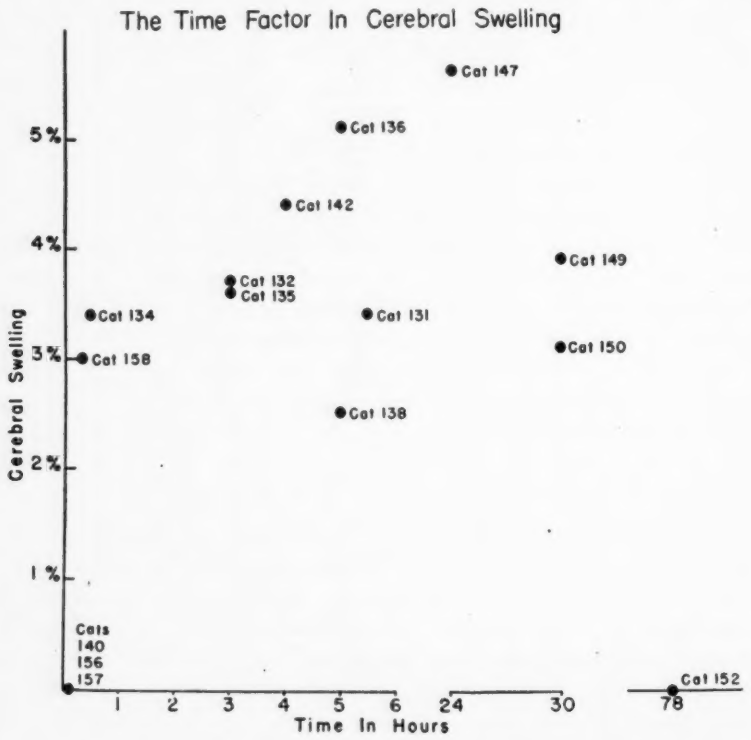

FIG. 2.—Relation between cerebral swelling and the time elapsed after concussion.

equally well to our findings after experimental trauma. During the first few minutes after the cat's head was struck the reflexes were abolished and consciousness would undoubtedly have been lost in an unanesthetized animal, as Williams and Denny-Brown[11] have demonstrated with the electro-encephalogram that the brain waves disappear over this period. But swelling is not an instantaneous process and did not develop to a measurable extent until all evidence of concussion had passed. Furthermore, as soon as the animals had thoroughly recovered from the anesthetic, they showed no evidence of discomfort or neurologic disturbance, in spite of the fact that cerebral swelling was at its maximum.

BLOOD VOLUME CHANGES AFTER CONCUSSION

Analyses of intracerebral blood volumes have been made in ten cats. Half of these were normal control animals, and in the other five the analyses

were made at periods of from 5 to 6.5 hours after concussion (the time at which brain swelling reaches its maximum). These determinations, recorded in Table II, showed no evidence of congestion of the cerebral blood vessels nor of extravasation of blood. The blood content of the brain varied from 4.33 to 0.44 cc., whereas in five normal animals it averaged 0.43 cc. These findings were corroborated by the microscopic examinations of sections of other traumatized brains stained with benzidine to bring out the erythrocytes (see section on "Pathologic Changes after Concussion").

TABLE II

CEREBRAL BLOOD CONTENT

Cat No.	Velocity of Blow: Feet per Second	Concussion	Blood: Cc.
*In traumatized brains:**			
159	45	++	0:37
160	45	+	0.23†
161	45	++	0.44
164	45	+	0.33
165	43	+	0.36
In untraumatized controls:			
167			0.36
69			0.49
70			0.57
75			0.40
105			0.36

* The traumatized cats were killed after 5 to 6.5 hours.
† Error probably due to inadequate grinding and extraction of blood from brain.

Both Pilcher,[4, 5] from his experiments on dogs, and Shapiro and Jackson,[12] from examination of brains of patients killed by cerebral trauma, concluded that posttraumatic swelling was largely due to an increase in the blood content of the brain. In Shapiro and Jackson's fatal cases cerebral contusion was severe enough to produce multiple petechial hemorrhages throughout the brain substance. But an increased blood content was not a factor in these cats with simple concussion, as chemical tests failed to show any increase in hemoglobin content and microscopic examination demonstrated neither petechial hemorrhages nor vascular engorgement.

CEREBROSPINAL FLUID PRESSURE CHANGES AFTER CONCUSSION

Determinations of the cisternal pressures were made in 14 animals, under light pentobarbital sodium anesthesia. In making these punctures the manometer was filled with isotonic salt solution to a point slightly below the normal fluid pressure. Eight cats served as controls and six others were submitted to trauma, all of which developed mild to moderate degrees of concussion (Table III). As it is a recognized fact that when two thecal punctures are performed with an interval of several hours the pressure in the second may be lowered because of leakage through the tract of the needle, we felt it best, as a rule, to perform only a single puncture and compare the pressure findings

TABLE III

HIGHEST RECORDED CISTERNAL PRESSURES IN CATS AFTER CONCUSSION

Cat No.	Velocity of Blow: Feet per Second	Concussion	Time after Trauma: Hours	Increase in Brain Volume: %	Cistern Pressure: Mm. of Normal Salt Solution
142	46.5	++	4	3.4	100
147	43	+	22½	5.6	75*
148	45	+	24	3.8	97
150	45	++	29	3.1	135
152	43	+	78	0	112
171	45	++	5	....	130

Cisternal pressures in eight untraumatized control cats under similar conditions: 55 to 90 mm., average 70 mm.

* Needle leaked.

in the traumatized animal with the average level in normal cats. In our eight control cats under light pentobarbital sodium anesthesia, cisternal pressures ranged from 55 to 90 mm. of isotonic salt solution. When postconcussional cisternal pressure determinations were made at intervals ranging from 4 to 78 hours, pressures were found between 75 and 135 mm. In the final observation on Cat No. 171 the cistern was punctured before the occipital blow and the needle then reinserted and left in place during a five-hour period afterward. The spinal fluid pressure rose from an initial level of 80 to 130 mm. (Fig. 3).

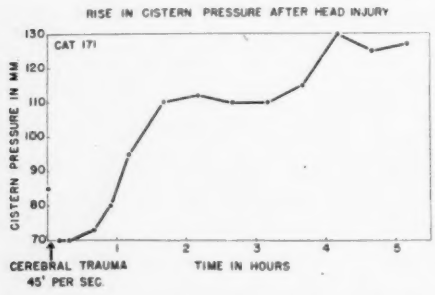

FIG. 3.—Rise of cisternal pressure in Cat No. 171 in the five hours following experimental concussion of moderate severity.

In spite of the small series of animals in which these readings were made, this evidence indicates that there is a slight to moderate rise in pressure after concussion and during the period in which the brain is swollen. The result in Cat No. 152 suggests that the elevation in pressure may outlast the period of actual swelling. In Pilcher's four dogs, where the fixed head was traumatized, there was also a comparable rise in the cisternal pressure readings. Our series is, unfortunately, small and it will be necessary to make further observations before exact conclusions can be drawn.

PATHOLOGIC CHANGES AFTER CONCUSSION

In the pathologic examination of these brains an attempt was made to demonstrate certain structural changes which could be correlated with the observed increase in cerebral tissue volume. Several investigators, among them Apfelbach,[13] and Courville,[14] have asserted that swelling of the oligodendroglia, enlargement of the perivascular and pericellular spaces, appearance of vacuoles in the white matter, hydropic changes in the cells of the ependyma and choroid plexus, are reliable indicators of traumatic cerebral edema. We,

therefore, prepared our material by technics best designed to show these alterations.

Immediately after removal, one portion of the brain was placed in formalin-ammonium bromide solution and the remainder in ten per cent neutral isotonic formalin solution. The duration of fixation was 12 days, after which sections were stained by Penfield's combined method for oligodendroglia and microglia; Pickworth's benzidine technic for the vascular tree; cresyl violet and H. and E. for cellular detail; Weil's method for myelinated fibers; and the Gros silver technic for axis cylinders. On many of the cases Sudan II (Oil Red O) fat stain was done.

The microscopic sections were examined without knowledge of the severity of concussion or degree of brain swelling. In each section a careful search was made for the aforementioned criteria of cerebral edema.

It was quite apparent that there was no significant difference in the vascular pattern or the amount of blood in capillaries and veins between the most severely concussed brain and those which were not traumatized. Swelling of the oligodendroglia was found only in Cat No. 132. This was surprising, in view of the constancy with which it has been observed in local brain edema and other states. Enlargement of the perivascular and pericellular spaces was noted in Cats Nos. 132, 136, and 147. Of these three brains, the amount of swelling in No. 136 was very slight. Hydropic changes in the ependyma was most conspicuous in Nos. 132 and 141; in the former concussion was rated as 2+, and the latter received no concussion. Vacuoles were present in white matter of Nos. 132 and 133, and were slight in No. 147. One of these (No. 133) had only a slight concussion. The sections prepared by the Gros silver technic for axis cylinders were examined particularly for swelling, tortuosity, and fragmentation of nerve fibers. In none of the experimental animals were these changes observed. From these data we are forced to the conclusion that these histologic criteria are unreliable and unsatisfactory for the demonstration of the degree of brain edema produced in this experiment.

To test the hypothesis of Mahoney,[15] that concussion is due to cerebral fat embolism, we made fat stains on several of the most severely traumatized animals. In none was there evidence of fat embolism.

DISCUSSION

Concussion, as recently defined by Gurdjian, Webster and Arnkoff, is "an unconscious state after head injury unassociated with macroscopic or microscopic lesions of the brain." If one may assume that the period during which the reflexes in these lightly anesthetized animals were abolished corresponds roughly with the period of unconsciousness, the disturbance produced was not severe. In the five animals permitted to recover from the anesthetic there were no signs of residual neurologic disturbance. Attempts to produce more severe grades of injury with definite contusion of the brain met with failure. Pendulum-striking speeds of 46.5 feet per second were the highest which the cats could survive. Such a blow was sufficient to produce linear

fractures in the occipital bone or bleeding from the ear, as well as hemorrhages around the medulla and cerebellum. Although this degree of trauma led to rapid death from respiratory failure in Cat No. 140, none of the three animals developed petechial hemorrhages in the gray or white matter, nor any other evidence of contusion. It is obvious that the small brain of the cat (average weight 26 Gm.) does not develop sufficient momentum to cause local bruising at the point of impact or by *contrecoup*. To accomplish this would require such a severe blow that the vital centers in the brain stem would fail to recover. The difference in vulnerability to trauma between the cat and the human brain is great. As shown above and by the experiments of Denny-Brown and Russell, it required a striking speed of approximately 20 miles per hour (30 feet per second) to produce concussion, and even rates of 30 miles per hour (44 feet per second) failed to produce prolonged disturbances in cerebral function. In man, on the other hand, falling from a hospital bed and striking the head on a hard floor has been a cause of concussion. At best, under these circumstances the head would undergo a free fall of three feet, and a striking speed of only 13.9 feet per second (9.5 miles per hour) could be attained. This greater vulnerability to trauma of the human brain is undoubtedly due to the larger brain mass and the contusing force derived from its greater inertia on sudden acceleration or its increased momentum on deceleration, not to any greater sensitivity on the part of the human nerve cells. As pointed out above, the histologic examination of the brains in these cats has shown no evidence of contusion. In man, contusion, and the obvious edema that may go with it, are limited to local areas where the bruising force has been exceptionally severe. It takes time to develop and cannot occur throughout the brain, because with such a severe injury death would be instantaneous.

After concussion it is evident that swelling of the brain follows much the same course as is seen in mild bruises in other parts of the body. It begins to appear within a quarter of an hour, reaches its maximum in from 5 to 24 hours, and subsides within three days. The quantitative method we have used in these and other experiments to measure cerebral swelling has given consistent results in over 100 animals, but one cannot differentiate between swelling of the cells themselves and extravasation of fluid into the intercellular spaces. For this reason we have refrained from specifying edema and have made use of the more inclusive term "cerebral swelling," but it must be emphasized that the permeability of the capillaries is not increased to the point where erythrocytes escape.

The swelling we have demonstrated after concussion does not seem at first glance to be very extensive, as it amounts to an increase in brain mass of less than 5.5 per cent. However, when one stops to consider the potential space available for expansion within the skull, it is evident that the intracranial cisterns and the cerebral ventricles must be definitely compressed. To understand this one must remember that the space within the cranium

contains not only brain tissue, but in addition the blood content of the cerebral vascular bed, the arachnoid and dural membranes, with the blood in the dural sinuses, and the cerebrospinal fluid which fills the remainder of the space. The quantitative relationships of these substances, in normal brains and also after concussion, are given in Figure 4. This shows that after a simple concussion the brain may swell to a point where it nearly fills the cranial cavity. The reason for the elevation observed in the cisternal pressures is, therefore, obvious.

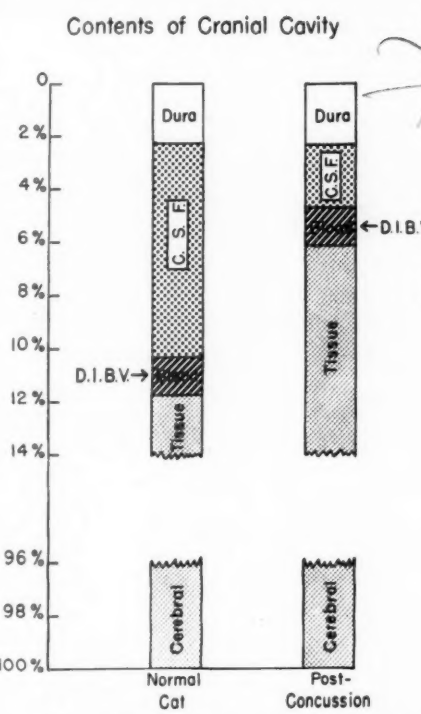

FIG. 4.—The relative space within the cranium occupied by the brain, its blood contents, the dura, and the cerebrospinal fluid. Before and after concussion.

Theories to account for the rise in intracranial pressure after head injury, expressed in previous articles (Pilcher[4, 5]; Arnaud[10]; Shapiro and Jackson[12]), have generally emphasized the importance of minute hemorrhages, congestion of the blood vessels, and the increase in intraventricular fluid, and have minimized the possible escape of plasma through the capillary walls. That an increase in intra- and extravascular blood plays an important rôle in cerebral contusion goes without saying, but it certainly is not a factor in concussion. Careful weighing of the residual fluid content in the ventricles after these brains were removed from the skull has shown that internal hydrocephalus is equally unimportant. We have, therefore, reached the conclusion that even in uncomplicated concussion there is a widespread extravasation of the noncellular elements of the blood through the capillary walls, although the process is so diffuse that actual edema or cellular swelling cannot always be visualized microscopically.

In the earlier paper by White, Verlot, Selverstone, and Beecher,[8] it was shown that anoxia, by itself, is capable of causing a 5 per cent increase in brain volume. Still further swelling may occur with a rise in the carbon dioxide content of the arterial blood. Hypercapnea is capable of producing such a congestion of the cerebral vascular tree that the blood content of the brain may be doubled. When these two factors work together, as they do during failing respiration and with an obstructed air-way, the cerebral volume may increase to the point where the entire available intracranial space is filled and the brain severely compressed. Whether cerebral swelling due to trauma is further augmented to a serious degree by complicating

factors, such as a failure of the respiratory center, obstruction to the air-way, and respiratory depressant drugs, is to be the next subject for investigation.

CONCLUSIONS

1. When cerebral concussion is produced in cats, for even brief periods, there is an increase in the volume of the brain up to a maximum of 5.5 per cent. The degree of swelling has been found to vary directly with the severity of the concussion. It makes its appearance in about 15 minutes, reaches its greatest extent between 5 and 24 hours, and subsides after three days.

2. Swelling of the brain is not related chronologically to the neurologic changes that accompany concussion. In these experiments it failed to develop until the respiratory, cardiac, pupillary, and corneal reflexes had returned to normal; and it reached its greatest extent after the animals had recovered from their anesthetic and no longer showed any evidence of residual cerebral disturbance.

3. After concussion the increase in brain volume is due to extravasation of fluid through the capillary walls, and not to the escape of red cells, to vascular congestion, or to distension of the ventricles with increased amounts of fluid.

4. The increase in cerebral volume reported has not been sufficient to produce the histologic changes which have been commonly regarded as characteristic of cerebral injury. There has also been no microscopic evidence of vascular engorgement or escape of red blood cells.

5. The degree of cerebral swelling is, however, sufficient to reduce the space occupied by the ventricular and subarachnoid fluid from its normal volume of 8 per cent of the intracranial cavity to 2 per cent. Coincident with this the pressure in the cisterna magna undergoes a slight but definite rise in pressure.

6. When there is, in addition, an area of contused brain, or when anoxia and a rise in the blood carbon dioxide level result from an obstructed air-way, failure of the respiratory center, or respiratory depressant drugs, further swelling and congestion of the brain may lead to serious compression of the vital centers.

We wish to take this opportunity to extend our thanks to Miss Anna Murphy and Miss Eleanor Fogerty, of the Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, for carrying out the blood-gas analyses.

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Discussion.—Dr. Francis Grant (Philadelphia, Pa.): This paper of Dr. White's represents a carefully controlled series of experiments. Of particular value are the results he has obtained in the production of more severe types of concussion. In experiments of this type in the past, control of the amount of applied injury has been difficult. The usual result in our experience has been that either little or no apparent damage has resulted from the blow or that the animal has promptly died.

To produce a state of prolonged unconsciousness in the animal that is at all comparable to the situation seen in man after severe cranial injury is very difficult, and only with the development of our ability to produce such experimental animals can we begin to study the fundamental causes of death following cranial trauma; why, for example, pulmonary congestion, hyperthermia and loss of peripheral vascular arteriolar control are so uniformly found in the terminal stages following cranial injury.

That a sudden, sharp movement of the head through space will cause unconsciousness is common knowledge. Many prize fights have confirmed this observation. But an abrupt deceleration in the movement of the head is much more serious. Then, a patient is thrown from an automobile or falls from a height, the movement of the head is suddenly and forcefully checked. Injury now occurs in two areas: At the point of immediate impact; and at the opposite pole, by contrecoup. The brain is shaken inside the cranial vault like dice in a dice box. Not only are there the coup and contrecoup injuries to the surface of the brain, but a case of contusion stretches into the midbrain between these points of injury.

Neither time nor inclination exists for the consideration of an exact definition of concussion. Many gradations of unconsciousness plus recovery come under this defini-

tion. We are all familiar with the football player who is knocked out momentarily, comes to his feet almost at once, plays magnificently in the last quarter, and on reaching the dressing room suddenly asks who won the game. He has no conscious recollection of anything that happened. He may and probably has had a concussion. He was apparently unconscious for a period but, then, except for his highest centers of memory and integration, he functioned apparently normally.

This is a situation which obviously cannot be reproduced in animals. But by this method of injury plus carefully coordinated studies of neurologic evidences of the degree of consciousness as shown by response to pain, abolition or retention of reflexes, plus microscopic indication of brain damage to definite areas, we may be able to determine, roughly at least, what degree of injury to what areas of the brain are necessary to produce the unconsciousness plus recovery we have termed concussion.

It is interesting in regard to these cases of Doctor White's that although the unconsciousness was immediate and the recovery was relatively immediate, the maximum swelling did not appear for some little time later on. So, obviously, the mild edema of the brain which he reported has had nothing to do with the momentary unconsciousness produced by the blow.

If I have any criticism of this paper it is that microscopic studies were focused on the presence or absence of evidence of edema and were not carried through the midbrain as well as the cerebrum at the point of application of the violence.

That the application of violence to the head was followed by edema is not surprising, even in the absence of evidence of contusion of the adjacent cortex. The brain responds to injury by a certain degree of swelling commensurate with the degree of injury, exactly as does any other part of the body. In man, concussion is commonly followed by a headache, suggestive of mild brain swelling which, just as in Doctor White's animals, begins promptly, may be maximal in 24 hours, and then disappear. It is to be hoped that those who believe in lumbar puncture or dehydration will note rather the rapid disappearance of this edema than its occurrence, and permit the pressure to subside spontaneously instead of trying to hasten its fall by unnecessary removal of fluid.

Doctor White is to be congratulated on this work. He has developed and improved the methods described by Zucherman and Denny-Brown, and confirmed their findings. It is through basic work of this type that our knowledge of the underlying physiologic processes consequent upon cranial trauma will be increased and possible advances in our treatment of these conditions made.

WAR WOUNDS OF THE CENTRAL NERVOUS SYSTEM *

CAPTAIN W. M. CRAIG, M.C., U.S.N.R.

THE RECOGNITION AND TREATMENT OF SHOCK, the use of the sulfonamides, the improved transportation of the wounded by air, land, and sea, and a more comprehensive conception of the physiologic effect of trauma have almost revolutionized the treatment of wounds of the central nervous system.

In previous wars the mortality in wounds of the brain was greatly increased by shock and infection. Transfusions of blood, plasma and albumin administered in sufficient quantities to combat shock have made possible the transportation of patients over long distances. The emergency treatment of open head wounds, consisting of shaving the scalp, arrest of hemorrhage and local application and oral administration of sulfonamides have allowed for an interval before reparative surgery is imperative of from 36 to 48 hours. These two factors have not only lowered the mortality and reduced the incident of infection but have changed the plan for the care of these cases. Hospitals far from the scene of battle can be utilized for reparative surgery and the patients transported to them. Postoperative care and rehabilitation can thus be carried out simultaneously.

Wounds of the spinal cord still produce marked disability, depending upon the severity of the lesion, but the factor of infection has been moderated. Spinal shock caused by wounds of the contiguous structures have been noted and under proper treatment have shown a tendency to recovery in a large percentage of cases.

Wounds of the peripheral nerves are, and will be, one of the major problems of the war. Injuries of the extremities comprise the majority of disabling wounds, and, naturally there is a high percentage of peripheral nerves involved. While at the present time an end-to-end anastomosis is the operation of choice, using nonabsorbable sutures, fibrin glue and nerve grafts are being investigated as to their efficacy.

Peripheral vasoneuropathy, or the so-called immersion foot, has been recognized as a disabling affection of the extremities occurring to men who have been adrift at sea. Degeneration of the peripheral nerves has been demonstrated in amputated feet and legs associated with pathologic changes in the veins and arteries. Adequate treatment has been followed by a minimum of permanent disability.

In the present war the ideal arrangement would be to establish neurosurgical centers at strategic points for the care of wounds of the central nervous system. However, because of the fact that our ships and hospitals

* The opinions or assertions contained herein are the private ones of the writer, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

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are so widely dispersed, this is impossible. While the Bureau of Medicine and Surgery have attempted to distribute the neurologic surgeons among the hospital ships and hospitals, it is important that physicians aboard ships, with the Marines, and at first aid stations, be made aware of some of the fundamentals of diagnosis and treatment.

A very definite program of instruction has been carried out at naval hospitals and particularly at the National Naval Medical Center, where series of lectures are given covering the subjects which a medical officer should know.

In attempting to teach some of the fundamentals involved in the effects of trauma, we conceived the construction of an animated diagrammatic motion picture which would depict the result of applied force. We were fortunate in having in our studio one of Walt Disney's assistants who had enlisted in the Navy. When outlining this motion picture the exact transmission of force to the head, causing the different types of injury to the brain, had to be demonstrated accurately. Simultaneously, with the drawings which were made, experiments were carried out upon monkeys in which the calvarium was removed and a lucite convex plate was applied over the brain. Motion pictures of the brain could be taken through the transparent cap showing the exact movements of the brain subsequent to the application of force to the skull. In this manner the drawings were made, and an animated, diagrammatic motion picture was made in the studio at the Naval Medical Center.

The motion picture illustrates the different effects of head trauma ranging from concussion to laceration of the brain. Depressed fractures which become infected through neglect or improper care, have been illustrated with the subsequent invasion of the meninges, the development of meningitis and brain abscesses.

Open and closed head injuries, with scalp wounds and penetrating wounds, are shown to emphasize the pathologic lesion.

As the proper treatment of head injuries, especially in the patients who are unconscious, requires free air passages, the effect of transporting the patient in the prone or the supine position is shown diagrammatically, with regard to the prevention of anoxia and its deleterious effect upon the cerebral cells.

The film illustrating head injuries is but the first of a series to show the effect of trauma upon the spine and to the peripheral nerves. It is being shown as an educational feature in the instruction of medical officers who are being sent out to care for the wounded aboard ship, in the mobile hospitals, and with the Marines.

Discussion.—Dr. A. W. Adson (Rochester, Minn.): I feel rather inadequate to discuss this paper, because our experience has had to do with patients in civil practice. I am very much impressed with the speaker's animated films and can see how valuable they are in the teaching of surgery.

I think perhaps I can appreciate the situation that confronts Doctor Craig and others who are called upon to teach special procedures to men with general surgical training. It is obvious that some of the teaching has to be rather fundamental, and certainly this method of teaching is a very effective one. Our experience with the

use of the silent movie has been most effective in teaching diagnostic methods and surgical procedures in neurology and neurosurgery.

I should like to emphasize one point, and that is the value of oxygen in the treatment of patients with craniocerebral injuries. We have found it to be of inestimable value in relieving the state of coma or unconsciousness.

Nothing has been said about chemotherapy. I am convinced that chemotherapy is a most valuable adjunct in the treatment of war wounds. The administration of the sulfa drugs in the presence of compound fractures of the skull lowers the incidence of meningitis and other septic conditions.

I congratulate Doctor Craig on the development of these animated films. I am sure that they will be worth while, not only in the development of neurosurgery but in the development of other phases of surgery as well.

DR. ALLEN O. WHIPPLE (New York City) : I do not pretend to discuss the neurologic phases of the subject, but I would like to say something about the possibilities of using the animated cartoon for certain types of teaching, as compared to the rôle which the so-called moving picture has had in the teaching of operative procedure.

I do not believe that we can teach surgery by the moving picture, at least the technic of surgery. That is too complicated a subject to teach by the moving picture. It always seemed to me it was like trying to teach a man to play the cello by a sound movie.

The animated cartoon, however, is an entirely different technic and offers certain possibilities which I think have not as yet been used. I speak particularly in regard to the demonstration of the embryology of the various systems.

We have with us, as one of our residents at the present time, a man who explored this field, to a certain extent, while he was a student at the Northwestern University Medical School, and he demonstrated, certainly in showing the development of the primitive brain, that it was possible to bring out certain features that are in chronologic order which cannot be demonstrated in any other way.

I am particularly interested in developing an animated cartoon of the development and rotation of the gastro-intestinal tract. I have to teach that about three times a year to the third-year students in Applied Anatomy, and I turn myself inside out and stand on my head three times a year trying to demonstrate the process to the students and I never get it across, but I know, in an animated cartoon, it can be done.

MR. JEFFREY JEFFERSON (London, England) : It is a great pleasure, naturally, to be here and to have the opportunity of hearing these discussions, to get a first-hand experience of the problems which suggest themselves to you as being most worthy of the focusing of attention, and to hear of the way in which you are attacking them, specifically in reference to this last paper of my old friend, Captain Craig.

Really, what Doctor Adson and Doctor Whipple said about the method practically covers the ground. I sat there, quite reinstructed again on some of the simplicities of surgery which always gave one pleasure to see at any time.

If I might, I would like to discuss a part of the paper which Doctor Craig did not give; that is, about the treatment of penetrating wounds.

Some of us, like myself, have had experience both in the last war and again in this, and we have been led to certain conclusions about them. I emphasize, I should agree with what Captain Craig said, of course, about the rapidity of the treatment, in which we all believe. But we are all astonished to discover that a number of patients treated with sulfonamide, particularly intravenously, survived untreated despite delays in further treatment due to circumstances of war. Of course, an aspect of all planning which is most difficult to get right, is the difficulties of any particular operation, not just any particular war, not just any particular exercise in one country rather than another, but the difficulties of a particular operation. While we all subscribe most heartily to the notion of early treatment, we add that the treatment should be given by competent hands and that a certain amount of delay is wise if by doing so the patient gets better treatment than he does by immediate operation by less skillful surgeons.

So it has come about that a number of patients have been successfully treated who had no operation at all for a matter of days. One has to resist the temptation to which some have succumbed, of concluding that perhaps we are quite wrong in thinking that early treatment is not necessary.

We have to avoid that. We have to watch and stick to our principles. Although even large numbers of patients should survive in this way there are probably a number of men who died by the wayside, of whom no record exists.

Then I come to the other point, and that is how one should best treat the penetrating wound. One thing has been apparent from all experience, and that is that suction is the most important of any surgical procedure that we have. That, as many remember, was introduced by Harvey Cushing in the last war, using a small rubber catheter. Even in many of our operations overseas, we have been able to supply them with power suction. The neurosurgeon, from his experience with the sucking out of portions of the brain and the section removal of the tumors, has been encouraged to suck out areas of damaged brain, a procedure which the general surgeon would have thought went beyond the boundaries of reason or perhaps of practicability. With the properly set apparatus it is possible to produce these large cavities, which permit filling with sulfanilamide powder. This is of great benefit to the patient in avoiding the draining sinuses or the edema, and allows for the subsequent rather low incidence of fungus.

Moreover, by doing so it is possible to remove all or most of the fragments and usually to get rid of the damaged tissue.

The last point is that most fatal infections are not cortical meningitis spreading from the edges of the wound, but an infection which has spread from the wounded area as encephalitis. To avoid the setting up encephalitis in damaged tissue, with the blood clot around about, one should completely excise this whole area by suction and leave that part of the wound as a kind of cavity, always closing the wound.

We have had some discussion as to whether or not scalp wounds, head wounds, and penetrative wounds should be left open or whether they should be closed, and although the general principle of leaving a limb wound, a flesh wound, open has been completely accepted by everybody, it has been no less completely accepted that head wounds ought to be closed. Some have closed them one, two, or three days after wounding, after the very thorough kind of suction and clean-out that I have mentioned, and have obtained something that is not perhaps quite primary union but very closely approximating it.

In this brief time I can not do full justice to this subject, but I thought that those were two points that occurred to me as being worth while of emphasis—they are, once more: The fact that those infections occur through an encephalitis that involves the ventricals and then spreads through all the ventricular passages, everywhere, rather than by local spread, and the necessity for the complete clean-up of the wound by suction, with the addendum that it is our duty to see that the surgeons who have to deal with these cases have the right instruments with which to carry out the operation.

CAPTAIN W. M. CRAIG, M.C., U.S.N.R. (closing): War wounds of the central nervous system have responded so satisfactorily to the modern method of treatment that it has become important to stress certain facts in the teaching of medical officers of the U. S. Navy.

At the Naval Medical School, where a course of instruction is given, we have been working on a plan of using animated diagrammatic motion pictures in emphasizing the fundamental factors involved in these wounds. Having Walt Disney's assistant in the enlisted personnel of the Medical Corps, and working in our motion picture studio, we have outlined a program for the making of motion pictures to be adapted to sound. This afternoon I am presenting the section dealing with head injuries.

These pictures are being presented as an educational feature in the instruction of medical officers who are being sent out to care for the wounded aboard ship, in the mobile hospitals, and with the Marines.

I greatly appreciate the discussion which has been made with regard to this presentation, particularly by Mr. Jefferson. I am sure you have all set up an experiment in the laboratory, and when you try the experiment you find it is not complete. Mr. Jefferson referred to penetrating wounds of the head. We spent months of our time on that portion of the film, which still remains on the reel, because, evidently, the film separated just as we reached the penetrating wounds, which I had hoped to demonstrate. He very graciously emphasized the points of importance.

RECENT ADVANCES IN THE TREATMENT OF RUPTURED (LUMBAR) INTERVERTEBRAL DISKS*

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RUPTURED LUMBAR INTERVERTEBRAL DISKS, discovered fifteen years ago, are now among the most common lesions coming to surgery. Their diagnosis and localization are simple, almost absolutely certain, and a cure is practically assured, and almost without risk. The story of the early development of this field is now well known but in the past three or four years both the diagnosjs and treatment have been revolutionized. Only these recent all important discoveries will be considered here.

The diagnosis can now be made solely upon the history of low back pain plus sciatica down the back of the leg and occurring in attacks: nearly always the backache and the pain in the leg are intensified by coughing and sneezing during the acute stage of pain. In 95 out of 100 cases with such symptoms a ruptured disk will be the cause. Three other conditions may cause the other five per cent: (1) Spondylolisthesis (2%); (2) congenitally defective fifth lumbar vertebra (2%); and (3) tumors of the cauda equina (1%). A roentgenogram of the lumbar spine will diagnose or eliminate spondylolisthesis and a congenitally defective vertebra. Tumors of the cauda equina (1% of the total), therefore, give the only problem in diagnosis. The symptoms may not differ from those of a disk but the backache may be higher, and there is frequently loss or diminution of patellar reflex. Should a tumor be present a lumbar puncture will usually show xanthochromic fluid. Only the suspicion of a tumor justifies a lumbar puncture.

Only two examinations are important: (1) Roentgenologic—In addition to excluding or diagnosing the above lesions, positive evidence of a disk is frequently indicated in the lateral view by narrowing of an intervertebral space. (2) The Achilles reflex: This is normal in over half the cases, but when reduced or absent, the disk is usually at the fifth lumbar. It is, therefore, important only for localization of the disk.

TYPES OF DISK

There are two types of disks: (1) Protruding; and (2) concealed (very slightly protruding or not protruding). The latter are twice as frequent as the former and it is their disclosure that has cleared the whole subject of disks. All of these will be missed if spinal injections of lipiodol, air, *etc.*, are used for diagnosis. Their symptoms are precisely like those of the protruding disks. They can be found at operation just as unequivocally as the larger disks. Always the nerve root is adherent and the thinned ligament

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

overlying the disk gives a sense of fluctuation to the forceps. When the ligament is punctured the forceps dip into a big cavity of the necrotic disk.

All affected disks have two components: (1) The necrotic interior; and (2) the part that protrudes or attaches itself to the nerve. The former causes the backache, the latter the sciatica.

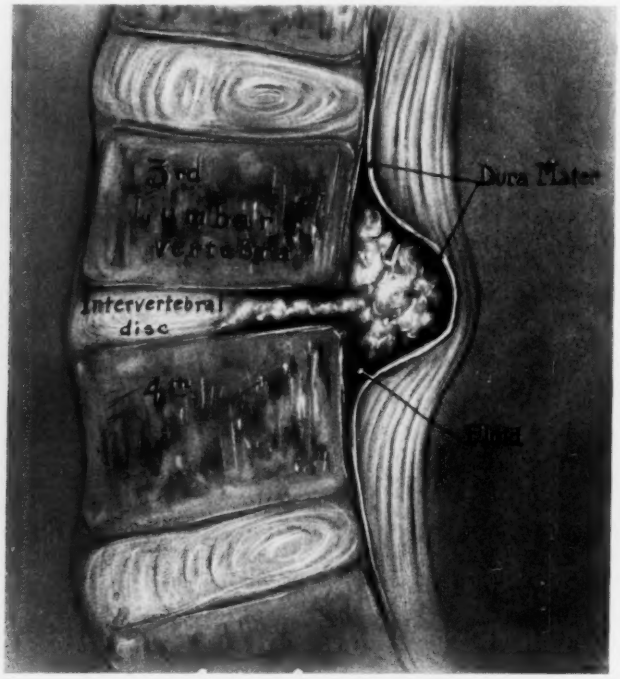

FIG. 1.—Drawing showing how the disk protrudes. The removal of the interior of the disk is all-important; unless thoroughly removed the percentage of recurrences will be very high.

SPINAL INJECTIONS OF LIPIODOL, AIR, ETC., CONTRAINDICATED

Until recently ruptured disks have been diagnosed and localized by spinal injections of lipiodol, thorotrast, air, *etc.* All are strongly contraindicated because they fail to disclose the small (concealed) disks which are two-thirds of the total. *All* disks can be diagnosed and localized without these contrast media, hence they are superfluous; moreover, if dependence is placed upon them, the two-thirds that do not show by the injections are denied the cure that surgery affords. Spinal injections are painful and unless the liquid contrast media are removed they are permanent deposits having free access to all the fluid-containing spaces of the brain. Even spinal punctures contribute nothing and should be avoided.

LOCALIZATION OF DISKS

Ninety-eight per cent of all lumbar disks are at the fourth and fifth. This was first shown independently by Love, at Mayo's, and Spurling, of

Louisville, and subsequent reports, including our own, have not changed this remarkable localization. This fact alone makes unnecessary any need for contrast media in the spine. It is almost as easy to explore both disks if it were necessary. But there are now methods of determining which of the disks is involved in over 90 per cent of the cases. If there is a diminution or absence of an Achilles reflex, the disk will be at the fifth in most instances. The roentgenogram shows a narrow interspace in many instances. When these tests are still negative, the affected disk can be localized at operation in

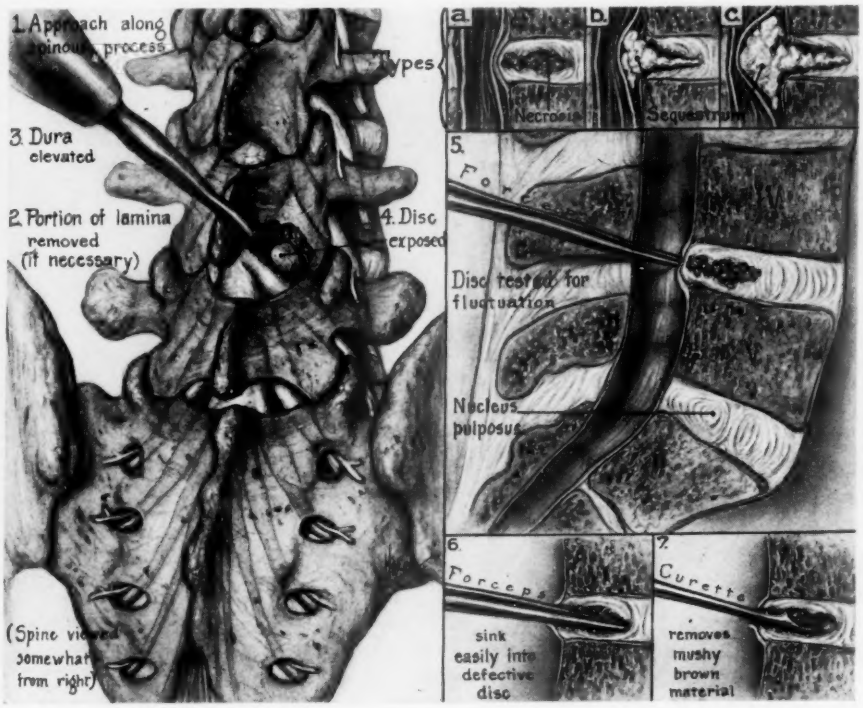

FIG. 2.—Drawing of a nonprotruding (concealed) disk. With experience, these are just as easy of recognition as the larger, protruding ones. The overlying ligament is thickened and white, and it fluctuates when the forceps press upon it. Moreover, it is usually quite adherent to the dura and nerve—at times quite densely so. When the forceps pass through the ligament a large cavity is entered; this is full of necrotic material—not infrequently large sequestra.

perhaps 85 per cent of the cases by horizontal pressure upon the spinous process. This determines the mobility of the joint, and a defective disk will nearly always cause an increased movement at the affected joint. The exceptions to this rule are in narrow intervertebral spaces shown roentgenologically; there may then be no mobility, or less than normal.

About 20 per cent of all patients with ruptured disks have two—one at the fourth and the other at the fifth. And since it is rarely possible to diagnose double disks before operation, the exposure of both is quite frequently done, especially when the increased mobility of the joint is demonstrable by pressure on the spinous process.

The unusual disks at the second and third are usually localized by pain in the front of the thigh; the others give pain in the back of the leg.

TREATMENT OF RUPTURED DISKS

The treatment of ruptured disks is dictated by the character of the pathologic process. Both the protruding disk and the necrotic interior

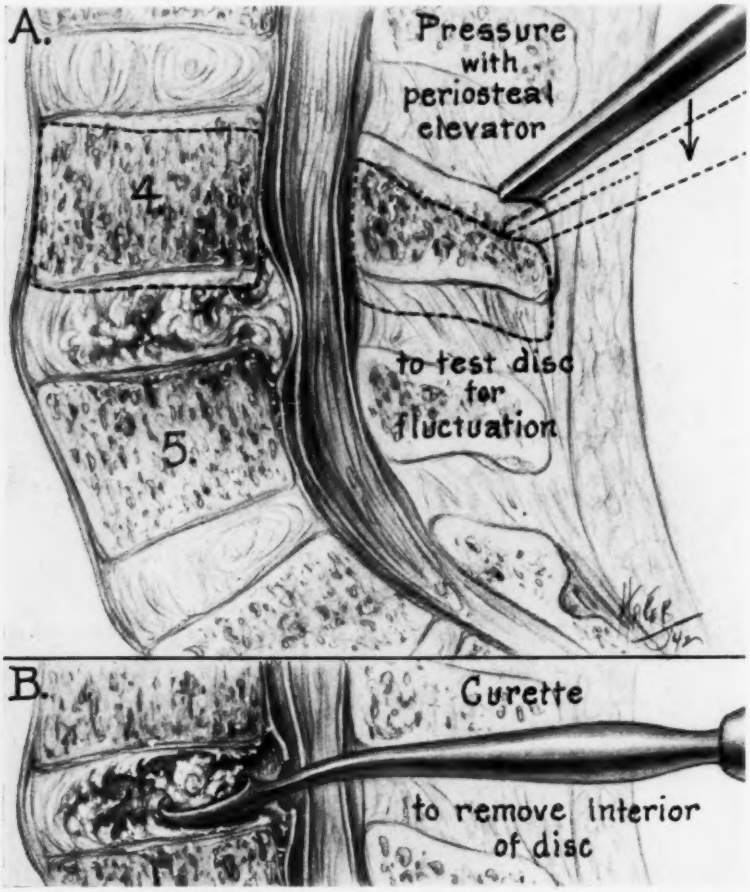

FIG. 3.—Method of removing the entire interior of the necrotic disk with a curette; this is done painstakingly and thoroughly. After this is accomplished firm fusion of the vertebral surfaces results.

of the disk must be removed. If only the protrusion is removed the backache continues and recurrence of sciatica reaches a very high percentage. The *cure* of a disk requires removal not only of the protrusion but of the entire necrotic interior of the disk. This is done by thorough curettement. If this is carefully done I do not think a disk can recur.

TREATMENT OF THE LATERAL JOINT

When there is excessive movement between the vertebrae, I have opened and curetted the cartilage from the joint on the side of the exposure. This,

unquestionably, adds to the stabilization but I am not certain that it is necessary. The surfaces of the bodies of the vertebrae after thorough curettement afford such a large area for fusion that fusion of the lateral joints is probably unnecessary. One such joint has been exposed five months later and was absolutely solid; nor was there any movement between the vertebrae which were very loose at the first operation.

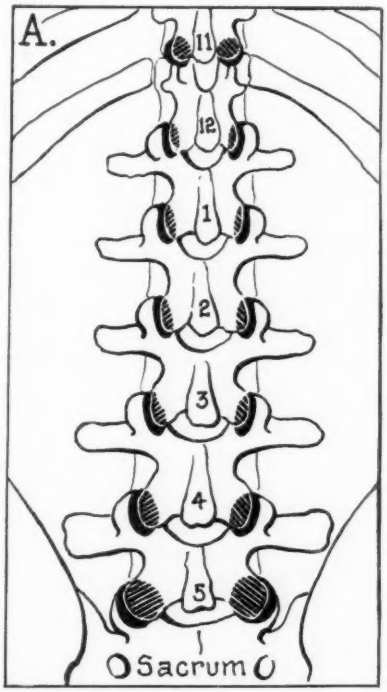

FIG. 4.—Schematic drawing showing how the lower three, particularly the lower two articular facets shift from the sagittal to an anteroposterior direction. This shift is least marked at three, more at four, and most at five. The degree of the shift varies greatly; it may be as much as 90° at the fifth lumbar. This change in the direction of the articular facets allows movement of the spine, but at the same time produces weakness and makes it susceptible to the development of defective intervertebral disks. There may also be marked asymmetry in the two sides.

CONCERNING SPINAL FUSION OPERATION

At the present time spinal fusions have attained a considerable vogue. The reason for this is that disks have been improperly treated in that the interior of the disk has not been removed. When the entire necrotic disk has been extirpated, firm union occurs between the vertebrae. There is no indication for fusion operations for ruptured disks and every reason for avoiding them. They require three months in a plaster encasement—a severe ordeal on the patient. The disk operation itself requires no encasement and the patient is out of the hospital in ten days to two weeks.

HYPERTROPHIED LIGAMENTUM FLAVUM

Frequently an operator claims the symptoms and signs of a presumed ruptured disk are due to a hypertrophied ligamentum flavum. This is merely a self-satisfying explanation for negative findings. A thickened ligament cannot cause these symptoms. Always there is a disk.

THE ANATOMIC REASON FOR THE FACT THAT NEARLY ALL DISKS OCCUR AT LUMBAR FOUR AND FIVE

The reason for this concentrated localization of disks to only the fourth and fifth lumbar vertebrae is, I think, explained on an anatomic basis. The planes of the articulations between the vertebrae change markedly at these two sites. Viewing the skeleton from behind it will be seen that the joints of the upper three lumbar vertebrae are parallel to the spinous processes. The plane of the fourth turns 45° and that of the fifth 90° from the horizontal. There are many variations in the degrees of rotation of the joints, the above being the maximum, but always this trend occurs and because of

this, greater movement of the spine—principally flexion and extension but some rotation—is obtained at these two points. The same transverse planes of the articulations occur in the cervical region where maximum movement is obtained. Disks also occur in the cervical region though less frequently because a lesser weight is superimposed.

RESULTS OF DISK OPERATIONS

To date, 506 disks have been operated upon. Always recognizing the importance of treating the interior of the disk, the treatment until recently had been only to break up the interior with an instrument and depend upon the subsequent spontaneous extrusion of the necrotic content through the surgical opening in the posterior ligament. The last 300 disks have been thoroughly curetted during the past year. Of these, there has as yet been no recurrence, but the time interval of one year is too short for comparison. However, I feel that recurrences should now be rare if the treatment is properly done.

The recurrences from the entire series are 25, or nearly five per cent. If the thoroughly curetted joints are excluded the recurrences in the series up to that time would be 14 per cent.

In the last 400 operations a disk has been missed only once—a tumor being responsible. In none of these has contrast media been used.

CONCLUSIONS

(1) Ruptured disks are among the most common lesions coming to surgery.

(2) Spontaneous cures must be very rare, although temporary remissions are the rule.

(3) There are two components of a ruptured disk: (1) The necrotic interior of the disk causing backache; and (2) the protruding portion causing sciatica.

(4) The diagnosis of a disk is made solely upon the signs and symptoms and roentgenograms of the spine. All disks can be diagnosed correctly and found at operation.

(5) Spinal injections of contrast media and spinal punctures are contraindicated; they are unnecessary and they will diagnose only one-third of the total number.

(6) The small (concealed) disks outnumber the markedly protruding ones two to one. They cannot show with any spinal injections of contrast media. It is the recognition of this group that has cleared the whole field of disk lesions. Their recognition at operation is unequivocal.

(7) Two disks in the same patient occur in about 20 per cent of the cases. Very occasionally there is a third disk.

(8) The exposure is unilateral and between the laminae, without removal of any bone whatever (Love's operation), or when the interlaminal opening is too small the removal of a small bite of lamina may be necessary.

(9) Mobility of the vertebra, tested by pressure on the spinous process,

will usually determine whether the disk is at the fourth and fifth lumbar (98 per cent are at these two disks), or at both.

(10) The entire necrotic content of the interior of the disk should be thoroughly removed with curettes. This is the best insurance against recurrences.

(11) Fusion operations are unnecessary and are contraindicated. Fusion of the vertebrae occurs after removing the necrotic contents of the disk. The articular surfaces can be curetted to induce further fusion in very loose joints, but I doubt that this is necessary.

(12) The reason for the localization of 98 per cent of the lumbar disks through the fourth and fifth lumbar is probably due to a shift in the plane of the articular processes from the horizontal to a transverse direction.

DISCUSSION.—DR. GILBERT HORRAX (Boston): Doctor Dandy has made such important and significant contributions to neurosurgery, as we all know, that I have some misgivings, as I think anyone would, in disagreeing with him on some of these questions which he has brought up, because he is a person of wide experience, and we all realize how much he has done to bring neurosurgery to the point which it has reached at the present time. As a matter of fact, I do agree with him on some of the points which he has stated here.

In the first place, I think all of us would agree that anything which simplifies diagnosis is important. If we can get away from lumbar punctures or from other types of procedures which are unnecessary, well and good, and insofar as we can, I say, all right.

Second, I would agree that the vast majority of the ruptured intervertebral disks in the lumbar region can be diagnosed by the symptomatology of the patients and the signs which they show. On the other hand, there are the two per cent, or possibly five per cent,—in our experience it is near five per cent—of disks which do not occur between the fourth interspace or the fifth interspace, which one has to account for and which one would like to diagnose more definitely, which I will come to in a moment.

I agree also, that now, there is little or no necessity for iodized oil. We have not used iodized oil at the Lahey Clinic for some years, having substituted oxygen for it, and we find, with experience, and with the cooperation of the Roentgenologic Department, that oxygen can be used perfectly well, and you can get comparable pictures to those which you obtain with oil.

I agree with Doctor Dandy about the removal of the interior of these disks. I think it is a very important feature that one must recognize and should aim to get out all the degenerated material that it is possible to obtain.

Again, I would say that, on the whole, fusions are very seldom indicated. We have a rule that after roentgenograms have been taken, if the patients show a very unstable lumbosacral region, with local reaction, irrespective of the disk, that those patients, almost certainly, ought to be fused, because such a fusion would cover a wider area than just the simple fusion which one does undoubtedly obtain by taking out the whole of the disks.

But now it seems to me that, from our experience, certainly, there are a great many patients who do not have the typical symptoms of a disk—the patients who have low back pain without the radiation down the leg in the sciatic area, in whom some form of further diagnostic procedure is necessary to determine whether or not a disk is present.

Furthermore, I would say that if one wants to get as accurate a determination as possible as to where the lesion is before operation—just the same way we use ventriculography, not always to diagnose a tumor but to get a more exact idea of its situation—so we find that the use of a contrast medium is advisable in that type of

case—the case that does not give typical symptoms, as well as to pick up the five per cent of patients who do have disks in other localities.

We have found, in addition to the ones in the fourth and fifth spaces, we have had nine out of 250 cases at the lumbar third, five at lumbar second, and two at dorsal twelve, in addition to three tumors, all of which had symptoms of ruptured intervertebral disks, and would not have been picked up without the contrast medium. But, as I say, anything which helps toward greater simplification of this problem is certainly commendable.

Dr. Albert Key (St. Louis, Mo.): We orthopedic men have been wrestling with low back pains for a long time, and patients with low back pain and with sciatica have gotten well and have stayed well for a long time, again and again.

I think that I agree with Doctor Dandy about lipiodol and also air. I do not like lipiodol and I cannot interpret air.

When his work first came out about concealed disks, I looked for them, and when I got through I was never sure whether I had made the disk and the cavity or it had been there. I did not realize the point that the nerve was always adherent, so I probably have looked in some normal disks for his concealed disks, and I felt that I had done a little more harm than I had good, and then I fused the spines.

Removal of the disk will not result in spinal fusion, that is by bony ankylosis between the bodies of the vertebrae. I think most of us have seen unstable lumbar spines with sclerotic opposing surfaces which caused symptoms.

In regard to the posterior fusion which is done by most orthopedic surgeons, we now keep our patients in bed only three weeks, and then let them get up with a belt or a low back brace. My criterion for an operation on the spine is a patient who has had the pain so long or is having so much pain that he justifies a major surgical procedure to get rid of it. Unless he is very markedly disabled and has had it for a long time, I do not think operation is justified. Lots of them get well with manipulations. Witness the popularity of the osteopaths. We have manipulated them long before we had osteopaths. Lots of them get well with rest and support. I think those should be tried first.

Dr. Walter E. Dandy (Baltimore, Md., closing): There is very little to add. Doctor Horrax has mentioned the fact that some of these disks occurred at the second and third lumbar interspaces. My criterion for a disk higher than the fourth is that the pain is in the front of the leg instead of the back. In my paper I was emphasizing the pains that occur in the back of the leg and not the front of the leg. If there is any question of its location, it can be determined by pressure upon the spinous processes; if the disk is at the second or third lumbar, there will be increased mobility of the affected vertebra.

The answer to the question, when to operate, is when they are having enough pain to seek relief. It must be realized that the complaints will probably recur for the remainder of life, for spontaneous cures must be very rare. There may be long remissions, but any little strain on the back reproduces the pain, and then it usually recurs with greater frequency.

I have exposed the site of earlier disk operations several times when the patient returns with a second disk; they are perfectly solid. This results because the whole surfaces have been extirpated, and a fusion of the entire bodies of the vertebrae is inevitable. As I indicated before, if the operation is done in that way, and done properly, I do not think a disk can recur.

OBSERVATIONS ON THE DISTRIBUTION OF THE SYMPATHETIC NERVES TO THE PUPIL AND UPPER EXTREMITY AS DETERMINED BY STIMULATION OF THE ANTERIOR ROOTS IN MAN*

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THE SYMPATHETIC NERVOUS SYSTEM, though nicely diagrammed in anatomical texts, has often been found by the surgeon seeking to effect sympathetic denervation of the extremities, to be apparently anomalous beyond all understanding in its devious origins and ramifications. This has been the case particularly with the upper extremities.

In a patient with Raynaud's disease that had had anterior rhizotomy, T.2 through T.8 on the right and T.3 through T.8 on the left, the observation 13 days after operation that skin galvanic responses were present in both hands led us to investigate further the spinal origin of the preganglionic fibers to the upper extremity in man.

It has been obvious that anatomic dissection does not suffice to indicate the physiologic pathways of the sympathetic nervous system. Neither can the information gained from animal experimentation, even in monkeys, be transposed to man. The contributions of trial surgical procedures of the sympathetic system in man have often been useful but just as often inconclusive and misleading. Witness, for example, the conflicting reports regarding the spinal origin of the preganglionic sympathetic outflow to the upper extremity in man. Gask and Ross[1] (1937) stated that the preganglionic sympathetic fibers for the arm extend from the segmental levels of the cord T.4 to T.9. Foerster[2] (1939), using the plethysmograph, made observations of vascular changes in the upper extermity on stimulation of anterior nerve roots. He concluded that the preganglionic fibers producing vasoconstriction in the upper exttremity exit *via* anterior roots T.3, 4, 5 and 6, and possibly T.7. White and Smithwick[3] (1941) gave the levels for preganglionic outflow for the control of blood vessels, sweat glands and erector pilae muscles of the arms as T.2 through T.8. Additional evidence[4, 5] has been supplied to show that T.2 is the upper segmental level for the preganglionic outflow in man. None of these observations has indicated that the upper level ever extends to the first thoracic segment and there is no uniformity of opinion about the lowest segmental level which may supply the upper extremity.

There has been less interest, though equal uncertainty, over the preganglionic outflow of sympathetic fibers to the pupil. Foerster[6] obtained homo-

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lateral dilatation of the pupil in man by stimulation of anterior roots C.8, T.1 and T.2. Hyndman and Wolkin[7] found that in five patients in whom anterior roots T.1 to T.5 were sectioned bilaterally, three patients showed bilateral miosis and ptosis, whereas two showed only unilateral changes.

Observations made on laboratory animals, chiefly the cat, dog and monkey, have indicated the variation in segmental levels of sympathetic innervation which may occur in different animals as well as in the observations of different experimenters and emphasized how unreliable are any attempts to commute the findings to man. Langley[8] concluded that the preganglionic outflow to the forelimb in the cat occurs in the fourth to the tenth thoracic nerve roots. Ascroft[9] found in monkeys that the segmental levels were T.3 through T.9. Kuntz, Alexander and Furcolo[10] concluded from experiments with cats and dogs that the "white communicating rami of the first and lower thoracic nerves include preganglionic fibers which effect synaptic connections with ganglion cells involved in the sympathetic innervation of the upper extremity." Sheehan and Marrazzi[11] have determined the preganglionic outflow to the upper extremity in the monkey by recording electrical activity of peripheral nerves during stimulation of anterior nerve roots and concluded that the outflow is limited to roots T.4 through T.8. Kuntz and Dillon[12] using the changes in the extremity recorded by a photo-electric plethysmograph following stimulation of anterior roots, maintain that in cats and monkeys the sympathetic outflow to the upper extremity has its upper level at the first thoracic segment.

By recording changes in skin resistance on stimulating the anterior roots Geohegan, *et al.*[13] determined the preganglionic sympathetic outflow to the limbs in cats and monkeys. They noted not only the variation from animal to animal but emphasized the difference in segmental levels of outflow that may exist on the two sides in a rhesus monkey. Their experiments were performed primarily to establish the validity of a method that could be used in the operating room for defining the origin of preganglionic fibers in man.

We[13, 14] have taken advantage of the opportunity to make observations at the operating table in 18 patients in whom the cervicothoracic region of the spinal cord was exposed for one reason or another. The tests were based upon the established fact that sympathetic nerves leave the cord *via* anterior spinal roots and that faradic stimulation of these roots causes sympathetic activity, one effect of which is a change in the electrical resistance of the skin in the area innervated. In some cases it was possible to stimulate the lower cervical and upper thoracic roots, in other cases the lower thoracic levels, and in still others the entire thoracic preganglionic sympathetic outflow to the upper extremity.

METHOD

The majority of the patients upon whom the observations were made were operated upon for relief of pain, the remainder had Raynaud's disease. Ether anesthesia was employed in all, and the preoperative dose of atropine was

limited to 0.0002 Gm. hypodermically. Fluids were administered intravenously throughout the operations in an effort to maintain the body's autonomic balance. In a few patients who developed even a moderate degree of shock the changes in skin resistance on stimulation of the roots were found to be unreliable.

A laminectomy was performed and the cord with its roots was exposed after opening the dura. The nerve roots were identified readily by skin markers over vertebral spines whose location was verified by roentgenograms before operation. Additional verification was afforded by postoperative roentgenograms showing the positions of silver clips placed in the dura at the foramina of the nerve roots. When the upper thoracic level of the cord was exposed, anterior root T.1 could easily be distinguished from T.2 not only by the difference in size but by the effects of stimulation—stimulation of the former resulting in muscular contractions in the hand and of the latter in muscular contraction of the back.

The anterior roots to be stimulated were successively isolated and held up on fine glass hooks. It was felt to be relatively certain that no spread of the stimulation occurred either to the cord or to adjacent roots. This was verified in many instances by obtaining sympathetic responses on stimulation of anterior roots after section of corresponding posterior roots or adjacent anterior roots, as well as by stimulation of the distal portions of transected anterior roots. Also, after positive results had been obtained, negative responses resulted when anterior roots were stimulated proximal to the point of crushing. In a number of cases simultaneous observations were made of the skin resistance in each hand and the positive responses were always limited to the side of the stimulation.

Two types of stimulation were employed, one delivered by a thyrotron stimulator and the other by a 60-cycle alternating current of about 2 r.m.s. volts measured under load. In the latter method the stimulus was derived from a simplified sine-wave stimulator, to be described later, and this method was found to be more desirable.

The changes in the electrical resistance of the skin of the fingers was utilized as an index of sympathetic activity. It is maintained by some[16] that the lowering of the skin resistance is dependent upon the synchronous development of both vasoconstriction and of sweating, occurring when either of these is present but being abolished when both are absent. Others[17] believe the skin resistance depends largely on sweat gland activity, being high when sweat glands are inactive and low when they are active. However, all agree that the lowering of skin resistance is a reliable indication of sympathetic activity and for our purposes this affords a convenient and reliable method for studying the sympathetic activity in man under the conditions imposed in experimentation at the operating table.

The changes in skin resistance were recorded by means of zinc electrodes fastened by finger stalls to the palmar side of the digits which had been cleaned with normal saline and wetted with saturated zinc sulphate solution. The

other electrode was fastened beneath the skin or to the exposed muscles of the back. In early experiments a Wheatstone bridge circuit was used in such a manner that changes in but one digit could be observed. Later, observations were made by a recorder built by Rahm Instrument Company, according to specifications developed by Geohegan. With this instrument it was possible to record graphically the changes in resistance occurring at two points of the body simultaneously. Thus, if simultaneous changes should occur in both hands following stimulation of the roots of one side such changes would be observed.

When electrodes were placed on various pairs of fingers of one hand it was found that a change in the skin resistance of one was always accompanied by a similar change in the other following stimulation of an anterior root. Thus, the stimulation of any anterior root containing preganglionic fibers to the hand resulted in simultaneous changes in all fingers of that hand and there was no suggestion of segmental innervation. This observation is in keeping with the conclusion of Billingsley and Ranson[18]; namely, that the preganglionic fibers of any given spinal nerve root have an extensive connection with the peripheral ganglia.

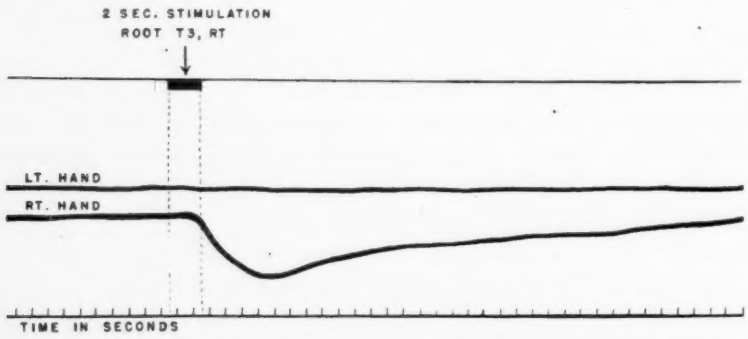

FIG. 1.—Record of skin resistance in the hands following electrical stimulation of anterior root T_3 on the right. The upper line represents the left hand—the lower the right hand. The downward deflection of the line indicates a decrease in skin resistance.

Unfortunately, stimulation of any of the anterior roots above T.2 causes movement of the extremity and distorts the recording of the skin resistance. However, the form of the wave (Fig. 1) and the latent period make it possible to distinguish between muscular movement and decrease in skin resistance. The former begins and ends with the stimulation and the wave fronts are sharp while the latter has a latent period of one to two seconds and the response is gradual and prolonged.

The pupils were observed for dilatation during each stimulation in order to establish the levels of their preganglionic innervation. These observations were possible in only eight of the cases in which the cervicothoracic segments were exposed.

RESULTS

The responses obtained from 16 patients in whom changes in the skin resistance of the hand were observed on stimulation of anterior spinal roots are summarized in Table I.

Of the 11 cases in which the highest levels of preganglionic outflow to the hand were investigated, ten showed the uppermost root of outflow to be T.2. In one case (Case 1), T.1 on one side contained preganglionic fibers to the hand and in another (Case 2), T.3 was the uppermost root of innervation on one side. Thus, in these two cases there was a difference in each person of one segment in the highest levels on the two sides.

Of the seven cases in which the lowest levels of preganglionic outflow to the hand were tested, the levels were variously found to be T.7, 8, 9 and 10. In two cases (Cases 12 and 16), there was a difference of one segment in the lowest levels on the two sides in the same person.

TABLE I.

SPINAL LEVELS FOR SYMPATHETIC CONTROL OF UPPER EXTREMITY

CASE NO.		T.H. 1	2	3	4	5	6	7	8	9	10	11
1	LT.	+	+	+	+	+	}	→				
	RT.	0	+	+	+	+		→				
2	LT.	0	+	+	+	+	}	→				
	RT.	0	0	+	+	+		→				
3		0	+	+	+	+		→				
4		0	+	+	+	+		→				
5		0	+	+	+	+		→				
6		0	+	+	+	+		→				
7		0	+	+	+	+	+	→				
8		0	+	+	+	+	+	→				
9		0	+	+	+	+	+	→				
10		0	+	+	+	+	+	+	0	0		
11		0	+	+	+	+	+	+	+	0		
12	LT.					←	{	+	+	+	0	
	RT.					←	{	+	+	0	0	
13					←	—	+	+	+	+	0	
14					←	—	+	+	+	+	0	
15					←	—	+	+	+	+	+	0
16	LT.					←	{	+	+	+	+	0
	RT.					←	{	+	+	+	0	0

TABLE II.

SPINAL LEVELS FOR PUPILLARY CONTROL

CASE NO.	C. 8	TH. 1	2	3	4	5
1	+	+	+	+	0	
2	0	+	0	0		
3	0	+	0	0		
4	0	+	+	0		
5	0	+	+	0		
6	0	+	+	0		
7	0	+	+	0		
8	0	+	+	+	0	
9	0	+	+	+	+	0
10	0	+	+	+	+	0

In two cases (Cases 10 and 11), the entire extent of the thoracic sympathetic outflow to the hand was examined.

In a few cases there appeared to be some difference quantitatively in the response to stimulation of various roots. Particularly was it noted that the

upper and lowermost roots were likely on stimulation to give a response of less degree than followed stimulation of the roots between. However, this was not a constant finding and the limited observations thus far make it unwise to conclude that these variations are of any significance.

The results of an additional study made in eight of the cases included in Table I and in two additional cases of the dilatation of the homolateral pupil on stimulation of anterior roots, are summarized in Table II. In one case (Case 1), the preganglionic outflow to the pupil was through anterior roots C.8 toT.3. In two cases (Cases 2 and 3), stimulation of root T.1 alone caused pupillary dilatation. In four cases (Cases 4, 5, 6 and 7), anterior roots T.1 and T.2 contained pupillary fibers; in one case (Case 8), it was roots T.1, 2 and 3; and in two cases (Cases 9 and 10), it was roots T.1, 2, 3 and 4.

DISCUSSION

The observations amply demonstrate the great variability in the segmental sympathetic innervation of the upper extremity and the pupil in man-variability not only in different individuals but between the two sides in the same individual.

Such information can be put to practical use in the diagnosis of the levels of lesions involving the cord or the thoracic sympathetic chain. It would explain, for example, the impaired sweating in the upper extremity (and in the face which probably has its innervation below T.1) with preservation of pupillary and palpebral function in the case of a paravertebral tumor (such as a "Pancoast tumor") which paralyzed all ascending components of the thoracic sympathetic chain below the first thoracic ganglon.[19]

We attempted to put the information to practical use in the treatment of Raynaud's disease with only partial success as far as total and permanent sympathetic denervation of the extremity is concerned. It was reasoned that the unfavorable late results in some patients, after one of the standard operations on the thoracic sympathetic chain, was probably due to the failure of the operation to prevent regeneration of nerves. The most popular operation, of recent time, has been that proposed by Smithwick,[20] in which, extraspinally, the second and third thoracic sympathetic gangli are freed from their central connections by cutting their rami communicantes and dividing the thoracic chain below the third ganglion. It was hoped that one advantage of dividing the anterior spinal roots which contained sympathetic fibers to the extremity would be to prevent or greatly minimize the possibility of regeneration.

In three cases (Cases 10 and 11 in Chart 1, and one other) all or all but one of the anterior roots on both sides, found by stimulation to possess preganglionic fibers for sympathetic innervation of the hands, were sectioned. The protocol of one of these cases will serve to illustrate what results were encountered.

In a patient with Raynaud's disease the skin temperature of the hands before operation, as recorded by a radiometer in a controlled temperature room at 25°C. approximated 23°C. in each hand. Block of the left stellate

ganglion with procaine was followed by vascular dilatation in the left hand and a skin temperature as high as 33°C. This demonstrated the ability of the peripheral vessels to dilate when released from vasomotor control. At operation, a lowering of the skin resistance in the hand was produced by stimulation of each of the anterior spinal nerve roots T.2 through T.9 on the left and T.2 through T.8 on the right. The anterior roots from T.2 to T.8 inclusive were cut on each side. Final stimulation of the intact T.9 root on the left still produced a lowering of the skin resistance in the left hand.

Twenty-one days later the skin galvanic reflexes induced by scratching the sole of the foot were absent in the right hand but present in the left. This demonstrated the presence of the remaining preganglionic innervation, presumably through root T.9 on the left side. Skin temperatures of the fingers on the right averaged 33°C and on the left 27°C. We interpret this to mean that the remaining anterior root T.9 on the left was sufficient to maintain the skin temperature 6°C. lower in that hand; yet as a result of section of the other anterior roots on the left that hand was 4°C. warmer than before operation.

Ten weeks after operation repetition of tests showed that skin galvanic reflexes were now present in both hands and the skin temperature had dropped to about 24°C. on the right and 23°C. on the left. The right ulnar nerve was blocked with procaine and the temperature rose in the ulnar half of the right hand to about 29°C.; no skin galvanic reflexes were now obtained in this part of the hand. This proves that sympathetic innervation had been reestablished on the right even though we had employed the usual procedure at operation of applying silver clips to the central and distal ends of sectioned roots.

We have assumed that the reestablishment of sympathetic innervation was probably not due to regeneration of cut fibers but possibly to some form of rearrangement or supplementation[21] of the outflow through roots not found at operation to possess fibers that caused changes in skin resistance when stimulated. However, regeneration of fibers from without into a ganglion may take place.

Thus, in addition to the variability in the segmental extent to which preganglionic fibers have been found present in man, must be added the observation that the interruption of all nerve roots found on stimulation to contain sympathetic fibers to the extremity in a given case may not be sufficient to effect permanent release in that extremity from sympathetic control. While the degree of sympathetic innervation which appears to be reestablished is not sufficient to affect materially in Raynaud's disease the benefits derived from multiple rhizotomy, the failure to cut all the roots originally found to contain preganglionic fibers is another matter. The case reported, in which the lowest root (T.9) was left intact, as well as another case in which the uppermost root (T.2) was spared, demonstrated that relatively little clinical improvement

occurred if but one of the six to nine roots containing preganglionic outflow to the upper extremity was left intact.

SUMMARY AND CONCLUSIONS

Knowledge of the preganglionic sympathetic outflow to the upper extremity and to the pupil in man has been incomplete, largely because it has been deduced by indirect methods or by attempting to commute the experimental observations in laboratory animals.

In a series of 18 patients in whom the cervicothoracic region of the spinal cord was exposed the anterior nerve roots have been electrically stimulated and observations made on the changes in the pupil and in diminished skin resistance in the hands.

Observations on changes in the pupil were made in ten patients and showed that the sympathetic innervation traveled through one or more roots and between the levels of C.8 and T.4.

In 16 patients in whom the levels of preganglionic innervation to the hand were investigated it was found that there was variation in the upper and lower levels within the limits of T.1 and T.10. This variation occurred from one individual to another, and on the two sides in the same individual.

In patients with Raynaud's disease division of all but one of the anterior roots found to possess preganglionic fibers to the hand resulted in preservation of much of the sympathetic effects in all parts of the hand and in but partial clinical improvement.

It was also found that after division of all anterior roots containing sympathetic fibers to the hand there was return of some sympathetic activity in that extremity by the tenth week. This is interpreted as possibly indicating a functional reorganization through other pathways.

The observations emphasize the necessity for recognizing the variability in the levels of sympathetic control to the upper extremity and pupil in man.

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ACUTE PUTRID ABSCESS OF THE LUNG*

VII. RELATIONSHIP OF THE TECHNIC OF THE ONE-STAGE OPERATION TO RESULTS

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AT THE PRESENT TIME there appears to be rather general agreement with the views we have set forth repeatedly concerning the desirability of operating upon putrid pulmonary abscess in its acute stage. There is no general agreement however, on the operative technic to be employed for acute abscess. There is advocated a variety of procedures such as the two-stage operation, cautery incision, intubation of the abscess cavity, partial or complete lobectomy, *etc.* The advantages (or disadvantages) of these operative technics cannot be analyzed logically because authors usually do not present arguments in favor of the procedures which they advocate. Thus, the reader is constrained to conclude that reported operative mortalities are chiefly or usually referable to an advanced or complicated stage of the disease which existed at the time of operation. Indeed, there is a tendency to classify acute abscess into "complicated" with higher, and "simple" with lower operative mortality. We propose (1) to present briefly the basis for the one-stage operation which has been employed in our clinic since 1925; (2) to describe the technic of the one-stage operation; and (3) to show that the operative mortality and morbidity as well as the late results of operation are related almost invariably to the operation and not to the disease.

(1) BASIS FOR ONE-STAGE OPERATION

The one-stage operation is based on the knowledge of the pathology of acute putrid pulmonary abscess and on the fact that anerobiasis plays an important (preponderant ?) rôle in the infection. The details of the pathology have been described elsewhere,[1, 2] In brief, an acute putrid abscess usually is solitary, of substantial proportions, superficially situated within the lung, and overlaid by well-developed visceroparietal agglutinating adhesions. By virtue of early liquefaction within the segmental area of gangrenous bronchopneumonia (which is the initial lesion) the abscess presenting the foregoing features exists as such within a week or ten days of the onset. The shell of lung overlying the abscess generally is thin, compressed, and avascular even in the earliest stages. Rare exceptions to the usual presence of agglutinating visceroparietal adhesions are to be found in abscesses facing fissures, the diaphragm, or the mediastinum. Under such circumstances overlying adhesions also exist but may be local and not visceroparietal. These are the unusual instances in which the free pleural space may have to be traversed

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in order to enter the abscess. All other abscesses can be opened at a one-stage operation without traversing the free pleura.

Precise roentgenologic localization of the abscess is an essential element of the one-stage operation and can, indeed, be regarded as the cornerstone upon which the one-stage procedure is based. Further reference to the subject will be made in the description of operative technic, but we may say here that, since the *only* means of knowing the site of contact of the abscess with the thoracic parietes (the site of adhesions) is precise roentgenography, the omission of exact roentgenologic localization of the abscess precludes the performance of a safe one-stage operation. Technically satisfactory roentgenograms cannot err; hence entry of the free pleural space at the time of operation (with the rare exceptions noted above) must represent an error in interpretation of films.

Even though a primary anaerobic origin of putrid pulmonary abscess has not been established unequivocally, there can be no question as to the importance of the anaerobic factor. The latter, according to all our experience, can be rapidly and completely eliminated only by liberal unroofing of the abscess. Thus, unroofing, not simple drainage, is an essential feature of the one-stage operation, and its performance under good vision usually can be carried out only at the primary operation.

(2) TECHNIC OF THE ONE-STAGE OPERATION

Since the technic of the one-stage operation is based upon precise roentgenologic localization, some consideration of the methods of localization is warranted. A study of properly taken postero-anterior, lateral and oblique films supplies the necessary information as to the situation of the abscess and its site of contact with the thoracic parieties. But it is at this point that the possibility, or at times the probability, of error begins. While it is true that in a few situations (thin individuals in which rib counting can be accurate, paravertebral abscesses in certain situations, anterior abscesses in the upper chest, *etc.*) the chances for error in localization are minimal, a margin of error always exists, and increases under a variety of circumstances (small abscesses, abscesses situated toward the axilla, abscesses in heavy-set individuals, abscesses partially or completely facing fissures, *etc.*). This gap between the true portrayal in roentgenograms and the possible, or probably, incorrect approach by the surgeon is completely bridged by the method of spot localization introduced by Rabin.[3] To outline the method briefly: After study of the films and fluoroscopy shortly before operation the assumed point of contact of the pulmonary abscess with the thoracic parietes is determined. The intercostal musculature at this point is injected with a small amount of a mixture of iodized oil and methylene blue. A new set of roentgenograms is taken. There is then revealed the exact relationship of the "spot" (of iodized oil) to the abscess. It may be directly over the abscess or as much as an inch away. The stain of methylene blue, which is in the same situation as the iodized oil, is exposed at operation. After it is revealed by an incision

down to the intercostal musculature one is in position to extend the exposure in the appropriate direction, and to the appropriate extent, in accordance with the relationship of the "spot" to the place of contact of abscess with chest wall. This ingenious method has made possible the precise operative exposure of many abscesses. It has failed in a few instances which, however, were the result of failure to inject properly the intercostal musculature. During the past two years the method has been employed in most operative cases, for we have learned that at times we may be as much as one rib off even in apparently simple cases. Local anesthesia is employed in practically all cases, except in young children. The subperiosteal removal of a two- or three-inch segment of one rib usually suffices. The excision of a section of an additional rib may be required for an unusually large abscess or, more often, because the primary exposure was not quite correct. As has been stated, adhesions are well-developed over the abscess at a very early stage. Other than in children, in whom adhesions tend to be rather tenuous, the absence of adequate viscero-parietal agglutinating adhesions comprises almost absolute evidence (exceptions already noted) of an incorrect exposure for an acute abscess. (In the subacute or chronic stages adhesions often are less firm and edematous). In recent years, we have often noted in the operative field the actual prominence and elastic feel of an abscess through presenting adhesions. We ascribe this frequent finding to greater precision in operative exposure, chiefly referable to Rabin's spot localization. The adhesions are delicately traversed over a small area down to adherent lung. This is done in order to be sure that the free pleural space is completely sealed off.

The abscess now is aspirated with a short aspirating needle which should be of a sufficient diameter to permit the withdrawal of thick, inspissated material. It cannot be too strongly emphasized that the abscess is superficially situated in the great preponderance of cases and that usually only a thin shell of lung is to be traversed in order to encounter foul air or pus. Here again, the site of aspiration is almost certainly incorrect if the abscess is found at a depth of more than a half inch. The overlying shell of compressed, avascular lung usually is about a quarter-inch in thickness and can be incised with impunity. The aspirating needle being held in place, we follow with a cutting grooved director and cutting scissors (Touroff[4]), urging the patient to avoid coughing at this stage. Once a clean entry into the abscess cavity is obtained the patient is permitted to cough if he wishes, and the contents of the abscess are evacuated by suction. Under full visualization the shell of lung over the abscess is generously excised within the limits of pleural adhesions. Bleeding from a pulmonary vessel, which is uncommon, can be controlled by a hemostatic suture. The result of the excision of the lid of pulmonary tissue should be an opening into the abscess almost as large as the cavity. Only in cases of large abscesses or in exceptional instances of limited pleural adhesions will the opening be appreciably smaller. An essential part of the operation is the unroofing of recesses in the abscess cavity,

which may at times require the incision of a thicker layer of pulmonary tissue, with occasional hemorrhage. Recesses are not rare, especially in cases operated upon in the fourth and fifth weeks, and their non- or incomplete unroofing at operation may result in persistence of the manifestations of pulmonary abscess. The disclosure of one or more bronchial fistulae is clear evidence that the main chamber of the abscess has been opened. A fistula often can be demonstrated by having the patient cough or strain. However, the orifices which are invariably present may be obstructed by blood clot or pus and, as a result, cannot be revealed at operation. The operation is terminated by gauze tamponade of the cavity. All recesses, as well as the main cavity, must be widely packed in order to avoid leaving behind foci of anaerobic infection. This essential step is facilitated by the use of narrow ribbon retractors and a sterile light placed into the cavity. Gauze strips are first packed into the recesses and then the main cavity is packed by superimposed strips of gauze. Tamponade is a correct term for the gauze pack of the cavity for the purpose is to avoid a collapse and consequent shutting off of any part of the abscess. An otherwise satisfactory operation may result in failure (so-called recurrence) if the precaution of wide packing of the abscess is not taken.

The entry of the free pleural space adjacent to adhesions, which usually is referable to an error in localization (at times to violent coughing or straining during operation) requires painstaking attention in order to avoid a possibly fatal putrid empyema. Placing a packing over a small opening into the free pleura does not suffice. When the one-stage operation is performed it is best to convert a small pleural opening into a larger one, for the lung adjacent to the abscess can then be broadly sutured to the thoracic musculature. The sutures should take deep bites into normal pulmonary tissue and there should be no pleural gaps after they have been tied. There should, however, be no tension on these sutures. After a gauze pack is placed and held in place over the suture line, the usual steps of the one-stage operation can be safely proceeded with. If, however, the pleural entry is not cared for by suture of the lung to the thoracic parietes a two-stage operation probably is safer. Thus, emphasis is placed on the desirability of recognition, frank acceptance, and fully adequate management of inadvertent entry of the free pleural space. Reference will be made later to the results of such management.

As has been stated, cases of pulmonary abscess in which adhesions are local and not visceroparietal (abscesses facing the fissure, *etc.*) are rare. Their satisfactory management by a one-stage operation at times presents difficulties, and, therefore, raises the question as to the desirability of a two-stage operation in such cases. Indeed, it will be noted that the fatal issue of one of our cases was in part referable to infection following a one-stage procedure. On the other hand, delay in opening a putrid abscess which goes with a two-stage operation invites serious and possibly fatal complications — spread of the abscess, spill-over infection to other pulmonary areas, pleural

contamination, difficulties in finding or in adequately unroofing the abscess at the second stage. The technic of the one-stage operation for the abscess in question should consist essentially of a liberal opening of the free pleura and the broad approximation by sutures of normal lung (adjacent to the abscess) to the thoracic parietes. For example, an abscess of the lower lobe faces the midportion of the long fissure and only local adhesions exist. The operative approach has been through the midaxilla and the free pleural space has been widely opened. Adhesions of the upper lobe to the interlobar surface of the abscess are freed in order to release enough of the free margin of the lobe for suture to the thoracic parietes. After this has been accomplished the surface of the lower lobe beyond the abscess is sutured to the musculature of the chest wall. The free pleural space is thus sealed off. After a strip of gauze is laid and held over the suture line the entry and unroofing of the abscess is proceeded with. A fortunately rarer abscess presenting a more difficult problem is one facing the diaphragm or pericardium. An extensive surgical procedure may be required. Thus, it may be necessary to expose and draw out of the wound much of the free border of the lower lobe and suture it to the thoracic parieties before proceeding with the unroofing of the abscess. The latter may be situated at a great depth and special precautions may be required in order to avoid pleural contamination.

Reference will be made shortly to the results of the one-stage operation for cases in which visceroparietal adhesions were absent.

Some reference must be made to postoperative management, for it is related directly to the operative procedure. The expectoration of foul pus (usually present before operation) should stop promptly after operation. Its persistence is evidence of an inadequate procedure. Since we are concerned here with the relationship of operative technic to results, it will suffice to point out that the inadequate operation must be followed by an adequate one if cure is to be achieved.

Assuming that the postoperative course and roentgenograms indicate that the pulmonary abscess has been adequately cared for, the problem of interest here is that of wound closure. We have learned that after an adequate operation the premature closure of an abscess cavity may, and often will, lead to recurrence of the manifestations of pulmonary abscess. The reason appears to lie in a tendency towards the persistence of anaerobic infection in the wounds. Therefore, the wound is kept open and the bronchial fistula maintained until the patient is free from cough and expectoration and roentgenograms establish the absence of pulmonary infiltration about the lesion.[2] Failure to adhere to these standards has led to recurrence of the pulmonary abscess, as will be recorded in some cases in our series.

A special problem exists in the case of unusually large pulmonary cavities which may be left after operation for large abscesses. The tendency toward early healing exists as in other cavities and must also be combatted. In addition, however, the closure of a large cavity may leave within the lung a considerable dead space. The potential danger of late infection within such

a dead space must be borne in mind, and we shall report one unfortunate case which will illustrate the point. We have employed free transplantation of fat in order to solve the problem of the large postoperative cavity which will not close, or which should not be permitted to close, because of the resultant large dead space.[5] On the whole, the results have been satisfactory although at times some dead space appears to remain (judging from the roentgenograms) when the fat graft becomes absorbed either as a whole or in part. The method is mentioned because we are concerned here with the question of the relationship of the technic of operation to the result.

(3) CAUSES OF OPERATIVE MORTALITY AND MORBIDITY

It will now be shown that the operative mortality and morbidity, as well as the late results of operation, are directly related to the technic of operation (and postoperative management) in the great preponderance of cases. Conversely, it will be shown that they are rarely related to the severity or extent of the disease. The following analysis can be regarded as timely because of the present-day tendency to ascribe operative mortality to the existence of "complicated" forms of the disease as well as to relate both early and late recurrences to the disease and not to the operation.

The one-stage operation which was performed in the great majority of our cases has, of course, been improved upon over a period of years. Thus, a few of the untoward results in our early experience almost certainly would not be seen at the present time. However, almost all cases have been operated upon in accordance with the principles and technic of operation which have been set forth, and all will be placed in the one category.

The series comprises 162 patients who were operated upon for acute putrid pulmonary abscess. There was no selection of cases, and many severe (hyperacute) cases are included.[6] There were four deaths, a mortality of 2.47 per cent. This mortality in an unselected large series in itself comprises evidence that death after operation can be rarely ascribable to the disease. The causes of death and the autopsy findings in the fatal cases have been detailed elsewhere.[7] Here, it should be pointed out that in three of the four cases the fatal issue was related, in whole or in part, to infection consequent upon errors in operative technic. In only one case, unique in our experience, in which a septic course continued unabated after a satisfactory operation, is death ascribable to the disease.

Turning now to the interval and end-results, it can be said, at once, that complications were few and that cure (in the sense of permanent freedom from symptoms and negative roentgenograms) was achieved in the great majority of cases. However, we are concerned particularly with complications and untoward sequelae in order to estimate their relationship to the operation.

Whether or not the free pleural space was opened at the one-stage operation postoperative suppurative pleuritis was extremely rare. It took place in one of the four fatal cases. There were two other instances in which empyema

followed inadvertent entry of the pleura early in our experience. They comprise errors in technic. Of special interest is the fact that there was not a single instance of pleural infection amongst all the cases (more than a dozen) in which the free pleural space was entered intentionally at the one-stage operation.

Reference should next be made to the small but important group of cases in which secondary operations were performed usually within a short time of the primary operation. The operations were required either for the enlargement of the existing opening into an abscess or for the unroofing of an adjacent abscess. In either case, the secondary operations are referable to errors in technic and not to the disease. Either the abscess was not adequately unroofed because of too limited adhesions or a recess or pathway leading to an adjacent cavity was not fully laid open. In two cases the results were unfortunate because the spread of infection made necessary repeated operations before a satisfactory result was obtained. Indeed, a chronic abscess ensued in one of them requiring prolonged treatment before cure was achieved. These two cases represent those exceptional instances in which overlying adhesions are not sufficiently widespread for adequate unroofing. The latter is an essential step of the one-stage operation, as already stated. Accordingly, it would have been better technic in the two cases to have opened the free pleura adjacent to the existing adhesions and to have approximated the lung around the abscess to the thoracic parietes over a sufficiently broad area for adequate unroofing of the abscess. Emphasis should be placed on the rarity of limited or delicate adhesions over the abscess. Such adhesions almost always point away from and not towards the site of contact of the abscess with the parietes.

The few instances of failure to recognize at operation a pathway to an adjacent locule (bilocular or even trilocular abscesses are not rare in the acute state of the disease) is strictly speaking referable to an error in roentgenologic interpretation and not to an error in technic. In any event, the secondary operation, which will almost certainly be required in order to achieve a cure, cannot be referable to the disease. Furthermore, purulent discharge from the wound and a few or many of the symptoms of pulmonary abscess which will almost certainly persist if the secondary operation is not performed, surely cannot be ascribed to the disease.

Secondary operations, consisting in laying open the original abscess cavity, were required in several cases because of premature closure of the wound. The intimate relationship between operative technic for and post-operative wound management of acute putrid pulmonary abscess has been emphasized. In a sense, therefore, this group of cases of secondary operations, due to recurrence of symptoms following premature wound closure, is ascribable to errors in technic. Such recurrences cannot be related to the disease. Nor can cases be so related when, after the patient leaves the hospital symptom-free after an adequate operation and subsequently the wound begins to discharge foul (or nonfoul) pus, fever returns, and symptoms

suggestive of recurrence of the abscess set in. As a practical matter, it can be said that meticulous attention to dressings following readmission of such cases usually will lead to the subsidence of all manifestations within a few days.

The operative technic for perforated putrid pulmonary abscess has a very direct bearing on the result. We are concerned solely with the pulmonary abscess of substantial proportions in which the clinical manifestations are essentially those of the abscess. Thus, there is the combined problem (according to the view we hold) of draining the pleural infection and unroofing the abscess even though a perforation, of sorts, exists (only rarely will the spontaneous perforation provide adequate unroofing of the abscess). There were several instances in which we believed patients to be too ill to withstand both wide drainage of the pleural infection and adequate unroofing of the abscess. In all of them secondary operations were required because of persistence or recurrence of the symptoms of pulmonary abscess. All these cases went on to cure but must be termed instances of inadequate technic at the primary operation. Similarly there were a few instances in which the pleural infection was not fully drained at the primary operation and subsequent thoractomy was required.

Finally, the relationship of the operative technic to late results requires consideration. A follow-up of all our cases, often over many years, has established the fact that permanent cure followed the described one-stage operation. Not all patients have survived, however. Death has been due to a variety of unrelated causes such as cancer of the stomach or of the bladder. In almost all these cases an autopsy was obtained revealing complete healing of the abscess and, thereby, providing incontrovertible proof of the relationship of the operative procedure to the result. There was another smaller group of cases in which autopsies made possible a complete study of the results of the one-stage operation. These were patients with chronic pulmonary abscess, operated upon for acute spill-over pulmonary abscess, who died subsequently from the effects of the chronic lesion. The postmortem examination in these cases revealed the same satisfactory findings in the operative field of the acute abscess as in the patients who died of unrelated causes. There are also several patients who are well, or improved, following operation for acute spill-over abscess complicating chronic abscess. In these the evidence obtained from roentgenograms indicates cure of the acute abscess. There also was a unique case of a spill-over acute abscess from an acute abscess in the opposite lung. Both abscesses were operated upon at the one sitting, and both are healed according to strict criteria.[8]

A late death calls attention to a problem which has not been solved by the technic of the one-stage operation, namely, the occasional persistence of a residual dead space following the operation for unusually large abscesses. We have described our efforts to prevent such residual spaces, including the transplantation of fat. The series of events in the fatal case was as follows: A one-stage operation was performed for an unusually large abscess of the

upper lobe. The postoperative course was entirely satisfactory. The residual cavity was soon clean. Because of its great size healing appeared unlikely. Accordingly, a free fat graft was implanted. Infection supervened, probably because of the unusual size of the graft; the fat masses were removed. The wound healed after five months and remained healed for three years of follow-up. Throughout this period the patient remained entirely well but there persisted in all films an area of rarefaction. The patient came under hospital observation six months later, with the history of a lung abscess of short duration. At operation, there was considerable difficulty in disclosing the abscess, which was finally found in the old dead space only after the free pleura had been entered. A putrid empyema developed which was drained. Death occurred, however, from the results of this infection and from cardiac failure. It was impossible to determine the duration of the pulmonary abscess. Since it occurred precisely at the site of the old lesion, it can be assumed that a low-grade infection existed which was lighted up by some undetermined cause. This assumption appears more likely than that of a new abscess. Accordingly, the case can be classified as being related to the technic of operation or postoperative care. There are several other patients who have been entirely well for years but who bear areas of rarefaction following operation for unusually large abscesses. Follow-up of these cases cannot be permitted to close, for it is conceivable that in other cases, too, late infection in the dead space may supervene.

Although this communication is concerned with the relationship of the technic of operation to the results in cases of acute putrid pulmonary abscess, it may not be amiss, in closing, to call attention to the fact that excellent results also have been achieved with the one-stage operation for cases of acute nonputrid pulmonary abscess. Since operation is more rarely indicated for nonputrid abscess, only 22 cases have been operated upon. All recovered, and the follow-up has established the existence of lasting cure in all.

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THE CHOICE OF OPERATION FOR DELAYED AND NONUNION OF LONG BONES*

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WHEN A FRACTURE of a long bone fails to unite after a sufficient interval of time, operative intervention is usually indicated. The object is to provide extra bone for the bridging of gaps, filling of defects and increasing stability, and to stimulate sufficient osteogenesis to result in bony union and to immobilize the fragments in a satisfactory position until union occurs. Other things being equal, the sooner the condition is recognized and treated the better the chance of success and the less the time lost by the patient. Consequently, early recognition of impending nonunion and decision on the part of the surgeon is advisable. However, he should avoid subjecting a patient to an unnecessary operation.

The decision when to advise operative interference may be relatively simple in a case with obvious interposition of soft parts or where several months or more have elapsed since the injury, or it may be very difficult in a borderline case, and the surgeon may err in either direction. Recently, I advised multiple drilling of a fractured tibia which had been treated by the two-pin method for eight weeks and then a plaster encasement for six weeks. There was slight distraction of the fragments and false motion on lateral strain. The patient refused the operation, and four months later union was not firm and the man is not working. This leg may unite eventually under conservative treatment, but I believe that the advice was sound and a relatively simple operation might have saved the patient months of disability.

A few years ago I would have waited until nonunion was unquestionable before advising operative intervention. This was because of the danger of infection. Now this danger is greatly lessened by implanting sulfonamide powder in the clean operative wound. Consequently, operations for nonunion are undertaken much earlier and many patients are saved months of disability and obtain better limbs than would be possible if operations were postponed until permanent nonunion was present. In addition to the sulfonamide in the wound, which I now use routinely in all operations, the patient is given sulfathiazole or sulfadiazine by mouth (one Gm. every six hours) for one or two days before and three or four days after the operation if the nonunion is present in a bone which has been infected during the preceding year.

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Now that operations for nonunion are performed earlier than in the past, the choice of operative procedure is broadened. In some instances the fragments are firmly held in good position and osteogenic stimulus is needed; in others internal fixation is necessary; and in a third group extra bone is indicated for filling defects or increasing the strength of the bone. The surgeon should choose the simplest operation which reasonably may be expected to yield a satisfactory result, and he should leave as little foreign material as possible in the wound. With the use of stainless steel and vitallium this is less true than in the past, but still it is advisable to use as little metallic internal fixation as possible, and this is especially true in bones which have been infected and in subcutaneous areas. Likewise, the simpler procedures are less apt to be followed by postoperative complications.

In the order of their complexity the operations which are most useful are: (1) Multiple drilling of the fragments; (2) open reduction and internal fixation, with or without multiple drilling of the fragments; (3) step-cut operations; and (4) various types of bone grafts, with or without other internal fixation. Each has its own sphere of usefulness and all should be followed by adequate external fixation—usually a plaster encasement.

1. Multiple Drilling.—This is useful in fractures where the ends of the fragments are in satisfactory position and are firmly bound together by dense fibrous tissue which may or may not contain cartilage. If the fragments are not in close contact or if they are bound together loosely so that they can be angulated easily or moved upon one another the operation cannot be expected to result in union. The procedure is especially recommended for oblique or spiral fractures because of the larger area exposed for drilling, but it seems to work equally well in transverse fractures provided the ends of the bones are in good position and are firmly fixed to one another by fibrous tissue or cartilage.

The drilling may be done subcutaneously through small stab incisions or under direct vision after exposing the line of fracture. About six years ago I drilled a simple fracture of the tibia subcutaneously and the operation was followed by a severe infection and extensive sequestration which necessitated two subsequent operations before satisfactory healing was obtained. Consequently, I now expose the fracture site and drill the bones under direct vision. Drills varying from $\frac{3}{32}$ to $\frac{5}{32}$ of an inch in diameter are used and several holes are drilled obliquely across the fracture line from each side and a few through the cortex near the end of each fragment, care being taken not to break up completely the fibrous union. The size of the drill varies directly with the size of the bone.

The wound is closed and the limb immobilized in a plaster encasement and treated as one would a simple fracture in the same location. Firm union may be expected in from six to eight weeks.

2. Open Reduction and Internal Fixation.—This procedure is useful in relatively recent fractures (from two to three months old) in which the

ends of the fragments are approximately normal in density. In such fractures interposition of soft parts or incomplete reduction or improper immobilization may account for the lack of union. If the ends of the fragments are sclerotic or atrophic or if they have been maintained in satisfactory position by either internal or external fixation over a sufficiently long period and have shown no evidence of bony union, it is probable that open reduction and internal fixation will fail and a bone graft is indicated.

At operation, the ends of the fragments are exposed and their margins

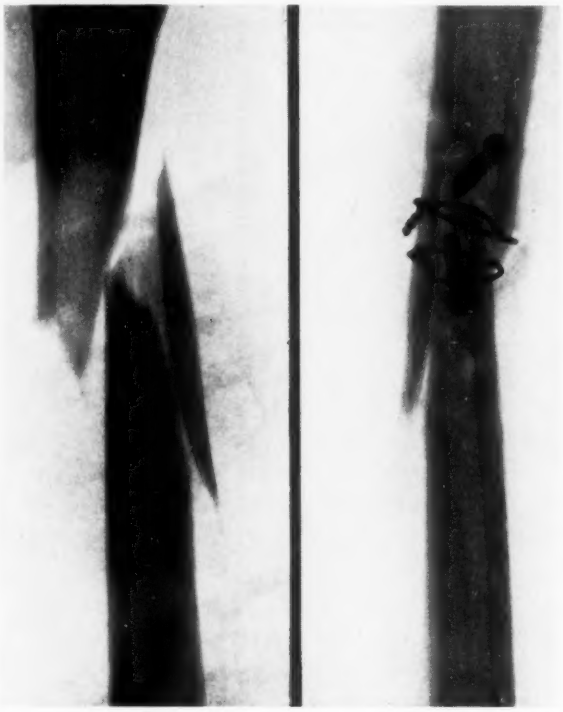

FIG. 1.—Left: Humerus with muscle interposition ten weeks after injury. Right: Same after reduction, freshening of ends, internal fixation and multiple drilling. Immobilized in a "hanging cast" for eight weeks; then active exercise until solid.

are freshened by pinching off the surface layer with rongeurs. The marrow canal of each fragment is opened and the fracture is then reduced and immobilized with noncorrosive wire or screws or a plate if necessary (Fig. 5). If large loose fragments are present they may be used as bone plates or splints (Fig. 1). No more metal than necessary should be used, but the fixation should be as rigid as possible. After fixation is complete a few small drill-holes should be made across the fracture line and near the ends of the fragments. The wound is closed and the limb immobilized in a plaster encasement and treated as would be a simple fracture in the

same location. Union may be expected to be somewhat slower than normal (eight to twelve weeks).

3. The Step-cut Operation.—In oblique or transverse fractures of the upper extremity, where a moderate amount of shortening is not very objectionable and which have not united after a reasonable length of time and where the bone ends are in fairly good condition, the step-cut operation

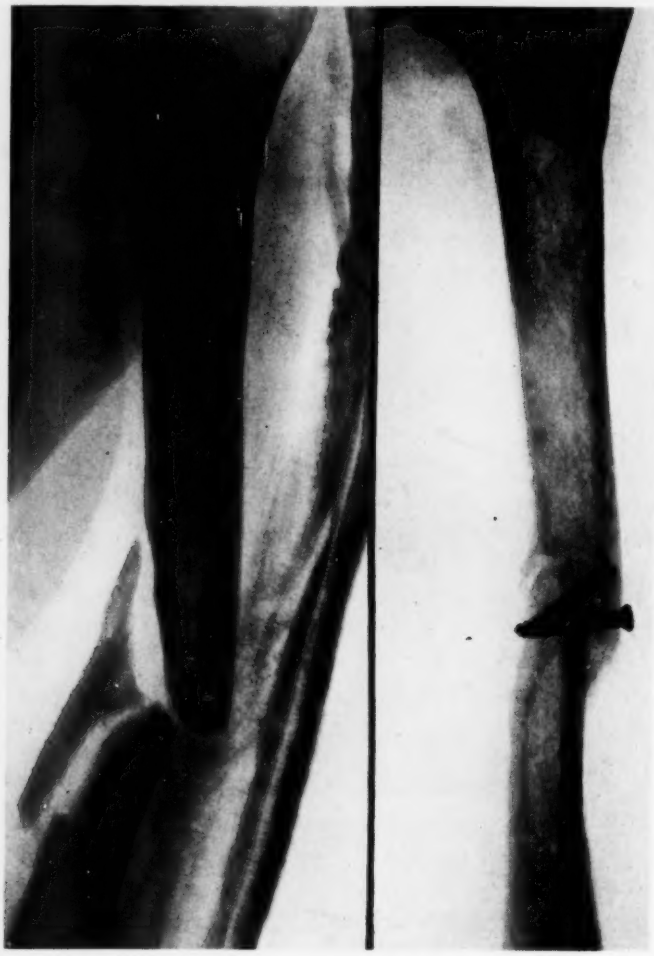

FIG. 2.—Left: Humerus with nonunion nine months after injury, with radial nerve paralysis. Right: Same after step-cut operation and neurolysis of the radial nerve. Immobilized in a "hanging cast" for eight weeks; then active exercise. The large loose fragment was removed.

offers a better chance of union than does the simpler open reduction and internal fixation. If the ends of the fragments are markedly sclerotic or atrophied the operation should not be used as it will probably fail to result in union.

At operation, the ends of the fragments are delivered into the wound

and the ends excised, preferably with a saw. Then, a small hole is drilled transversely across each fragment about one inch from the end and, with a saw, a step-cut is made in the end of each fragment to form a tongue including a little more than half of the diameter of the bone. The step-cuts are on opposite sides so that when the ends are pushed together and fastened by two noncorrosive screws placed at different angles they form a fairly stable union (Fig. 2). If necessary the marrow canals are opened before the step-cuts are made and drill-holes are made in the bone near the step-cut. Drilling of the ends of the fragments is usually omitted as it would weaken the bone which is only half its normal thickness. A few bone chips or splinters from the excised bone are placed around the fracture and the wound is closed. The limb is immobilized in a plaster encasement and treated as would be a simple fracture in the same location. Union may be expected in about the normal time (six to ten weeks).

FIG. 3.—Anteroposterior and lateral views of tibia fractured when the patient fell from a high curb. A large graft had been removed two months before the injury. This fracture healed slowly.

4. Bone Grafting Operations.—Bone grafting operations are used in those instances where it is believed that there is a probability that the simpler procedures mentioned above will not be successful. This is because the use of a bone graft usually increases the gravity of the operation about one-third. It is assumed that the graft is to be an autogenous graft because, while various substitutes for the autogenous graft have been used, I do not believe that any of them actually stimulate osteogenesis. Consequently, if a graft is indicated it should be an autogenous graft. This necessitates a lengthening of the original incision or a second incision.

In many instances in fractures of the leg the graft can be removed from the fractured bone, and I have seen no evidence that this decreases the probability of union of the fracture, and if the operation is on the lower extremity this offers the advantage that the opposite sound leg is not

temporarily crippled or weakened. That this weakening of the sound leg is an actual hazard if a large graft is removed is evidenced by Figure 3. This leg was fractured by relatively slight violence about two months after the operation, and took longer to heal than did the opposite leg which

FIG. 4.—Top: Radius and ulna reduced, wired and drilled six weeks after the injury. A previous open reduction had failed to maintain position. Below: Radius and ulna five months after fracture. A previous open reduction and wiring of fragments had failed to secure union. Intramedullary and splinter grafts and cancellous bone in each and ulnar fragments held by wire. Immobilized in a plaster encasement for ten weeks.

had been grafted (Fig. 8). This, in spite of the fact that spicules of bone had been curled up from both margins of the defect to hasten the filling in my bone of the defect created by removal of the graft.

Notwithstanding the fact that the use of a bone graft increases the

gravity of the operation, it will be found that a graft is indicated in most instances where more than three months have elapsed since the injury. The principal exceptions are fractures suitable for step-cut operations or multiple drilling.

Source and Type of Graft.—If it is not feasible to remove the graft from the broken bone adjacent to the field of operation, it must be removed from some other bone. The tibia is usually chosen because it presents a large flat subcutaneous surface from which the graft can be cut with a

FIG. 5 FIG. 6

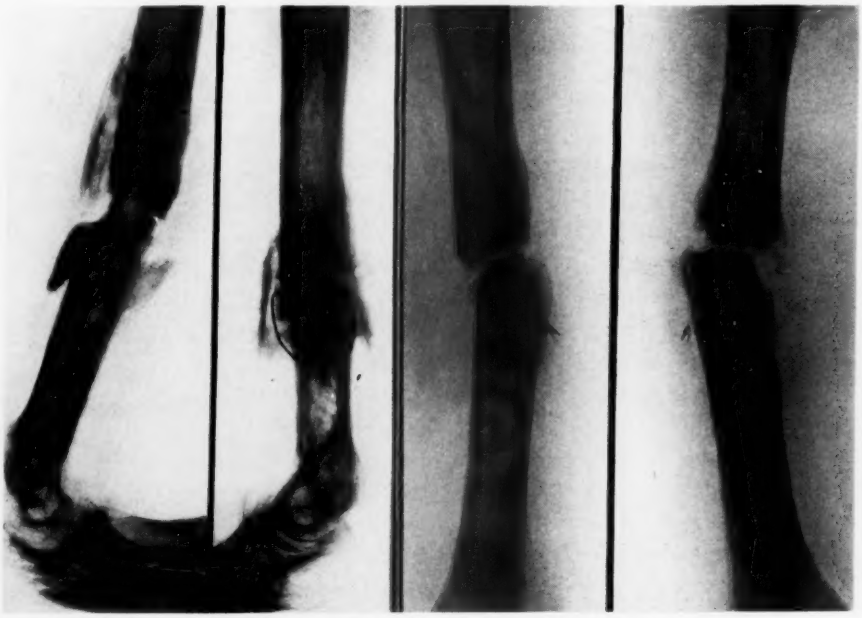

FIG. 5.—Left: Nonunion of humerus after three operations. The radial nerve was then sutured and a step-cut operation was performed by the author, but still the bone did not unite. Right: Same after an intramedullary graft and wire loop, with splinter grafts and cancellous bone. Union was quite firm after eight weeks in a "hanging cast."

FIG. 6.—Failure of an autogenous intramedullary peg for nonunion of the humerus, the remains of which can be seen in the marrow canal. A wire loop might have made the difference between union and failure.

motor saw with relative ease. If only cancellous bone is needed this is best removed from the ilium. In unusual instances where an extensive defect is to be bridged, as much of the shaft of the fibula as desired may be excised without causing serious disability in the leg.

In deciding upon the type of graft to be used in a given case, the functions which the graft is to perform must be considered. Compact bone is strong and also has considerable osteogenic properties. Consequently, it is the type of bone most frequently used, and this is especially true where it is desirable that the graft provide some internal fixation. Cancellous bone, bone chips and slivers and osteoperiosteal grafts have more osteogenic

power, but offer little in the way of fixation. They are most useful in operations for arthrodesis and in filling defects or in combination with some form of internal fixation (plates, screws or wires, or as adjuncts to cortical bone grafts).

It having been decided that a bone graft is indicated, the surgeon must decide what type of graft will most satisfactorily solve the problems presented by the particular fracture to be operated upon. If the graft is to furnish internal fixation it should be of cortical bone and may be of the massive onlay type of Campbell[1] or Henderson,[2] the inlay or the wedge graft of Albee,[3] the medullary inlay of Buchanan,[4] the double onlay of Boyd,[5] the intramedullary graft of Ryerson,[6] or the massive sliding graft of Gill.[7] All of these are useful in bridging defects in the bone.

If internal fixation is not to be furnished by the graft, one may use the splint graft of Phemister,[8] the multiple barrel stave grafts of Steel,[9] the cancellous bone grafts from the ilium of Abbott,[10] the osteoperiosteal grafts of Ollier or small slivers of cortical bone or bone chips and fragments of cancellous bone and endosteal bone placed around the line of the fracture and between the ends of the fragments. This group is especially useful when combined with internal fixation by noncorrosive metal plates, wire or screws, and in instances where metal is to be avoided because of recent infection or infection present at the time of the operation. They are also useful adjuncts to multiple drilling operations.

Technic.—In the usual case of nonunion of a large bone of several months duration with sclerosis of the bone ends and a pseudarthrosis or flexible fibrous union, I prefer the massive onlay graft of Campbell or Henderson, but use the entire cortex of the bone, do not prepare a flat bed, and fix the graft with metal screws (Key[11]). In preparing the site for the graft the ends of the fragments are exposed subperiosteally and the dense fibrous tissue around and between the fragments and the adjacent sclerotic bone is excised. The marrow canal of each fragment is opened by removal of the plug of eburnated bone which occludes it. The fragments are then remodeled and placed in a satisfactory position and if possible an end-to-end apposition is obtained.

It is often stated that as little periosteum as possible should be removed from the ends of the fragments, but I have exposed the ends rather generously and have not seen that it did any harm as fairly prompt union has always followed this operation. With the exception of congenital fractures my failures have occurred in patients in whom I have used some other operation. In some instances the fellow bone of the leg or forearm is cut obliquely and shortened or a cross section is removed in order to reduce or eliminate the space between the ends of the fragments.

The site of the graft, usually the anteromesial surface of the tibia of the opposite leg, is exposed subperiosteally and the graft is excised with a motor saw. Before cutting the graft the holes are drilled for the screws. These

are slightly larger than the metal screws in order that the graft may be screwed tightly against the bone. Then, the graft is firmly fixed to one fragment with two or three metal screws and the other fragment is then placed in position and the graft also fixed to it. A series of small drill-holes are then made near the end of each fragment (multiple drilling) and

FIG. 7 FIG. 8

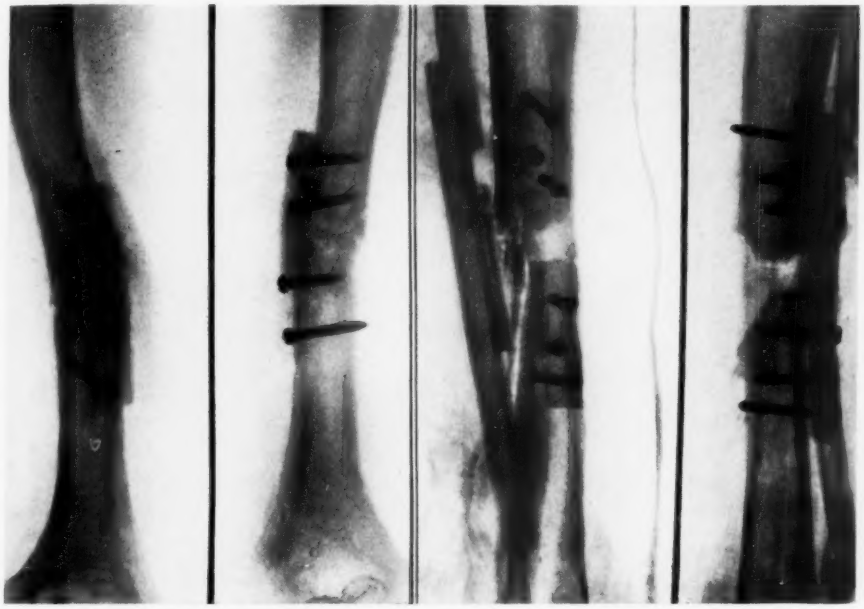

FIG. 7.—Same eight weeks after onlay graft, plus cancellous bone and splinter grafts, and drilling and opening of the marrow canal. Had been immobilized in a "hanging cast." Union was firm.

FIG. 8.—Old nonunion of the tibia, with loss of substance. The leg was shortened about one-half-inch by sliding the fibula up, and the fragments were fixed with an onlay graft and drilled and the remaining defect filled with cancellous bone and bone splinters and chips. Immobilized in a plaster encasement for three months, until union was firm. In the meantime the patient fractured the other leg (Fig. 3).

several small pieces of the cancellous bone from the proximal end of the tibia are scooped out with a large curette or gouge and are pressed down against the fracture line. Also, two or more small slivers of bone are cut from the margin of the defect from which the graft was taken and are placed across the fracture line on the side of the bone opposite the graft. If there is a space between the ends of the fragments, this is packed with cancellous bone and bone chips. Slivers of bone are then curled up from the side of the graft defect in the tibia and the wounds are closed and the extremity is immobilized in a plaster encasement (Figs. 7, 8 and 10).

The onlay graft is then a bone plate of heavy cortical bone. In recent years I have sometimes reinforced the graft with an oblique screw, as used by Darrach and Murray in their bone-plating operations in order to increase the rigidity of the fixation (Fig. 11). This operation has certain

Fig. 9

Fig. 10

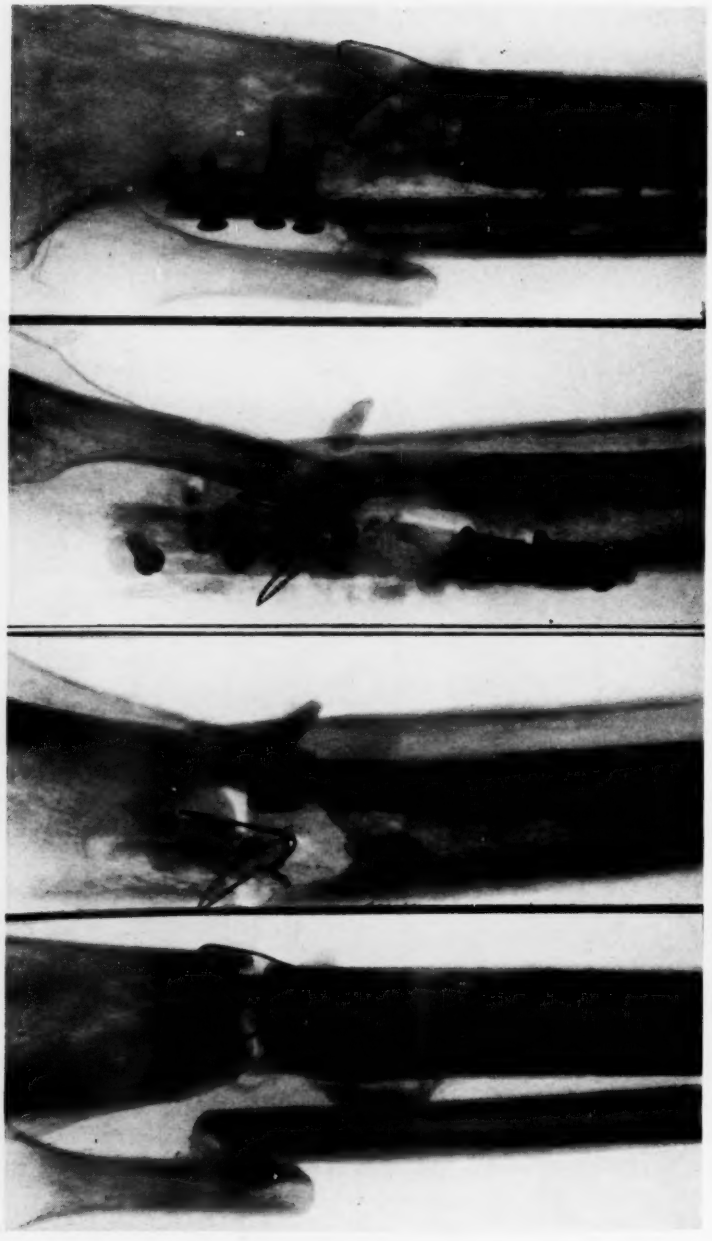

Fig. 9.—Old nonunion after open reduction and wiring.
Fig. 10.—Same after onlay graft, multiple drilling and accessory bone to fill the dead space beneath the graft. The wires were not exposed. Immobilized in a plaster encasement for ten weeks. After union was firm a sinus developed on the mesial side over the wire. This and the screws were removed, and there has been no further trouble.

disadvantages and limitations. Due to the considerable amount of metal left in the wound it should not be used in infected or recently infected bone if some other type of graft offers a fair chance of success. I have recently removed the screws from a Buchanan-type of graft done about three years ago. This was an old infected compound comminuted fracture and the graft was laid in the medullary canal of the distal fragment because much of the cortex was lost. Over two years later a low-grade infection developed around one of the stainless steel screws. As it increases the thickness of the bone by the size of the graft it should not be used in subcutaneous areas, and is rarely used in the forearm. It is preferably used on surfaces well covered by muscle. Due to the fact that at least two screws should be placed in each fragment it is not suitable if one fragment is quite short as it may interfere with the movement of the joint.

In spite of the objections mentioned above, I consider the onlay graft, as described above, as the standard operation for nonunion of long bones. In my hands the inlay graft has not furnished very secure fixation and it has been reserved for subcutaneous areas, such as the malleoli and the distal third of the leg and forearm.

During the past year, or longer, we have been experimenting with the massive onlay graft placed posterior to the tibia, without internal fixation. The operation is attractive because of its simplicity. It is suitable only in instances where the fragments are in satisfactory position and fixed by fibrous tissue; that is, cases where multiple drilling might result in union, but where a little extra stimulus to osteogenesis is desired. An incision is made along the posteromesial border of the tibia and, with a sharp osteotome, thin slivers of bone and the periosteum are elevated from the posterior surface of the bone at the line of the fracture and a short distance on either side. This provides a flat bed of raw bone for the graft with periosteum and some bone over it. Then, a relatively wide, short full-thickness graft is removed from the proximal third of the anteromesial surface of the same or the opposite tibia. The fat is wiped from the endosteal surface and with this surface next to the tibia one end of the graft is driven upward and inward behind the tibia. The lower end of the graft is then pushed in and driven home with a nail set. Several holes are drilled across the fracture line and bits of cancellous bone are pressed in around the fracture line and the wound is closed. (Figs. 14, 15 and 17). We have called this the Phemister graft because it is similar to the method described by him a few years ago. Phemister[13] used it in all long bones and even in bones which were infected.

We have also used multiple thin grafts of cortical bone placed across the fracture line around the bone (the barrel stave grafts of Steel), but where we have used these we have also used a bone plate for internal fixation (Figs. 18 and 19) and have on one occasion used the thin cortical bone graft beneath a noncorrosive plate as advocated by McBride.[14]

The above operations all resulted in union in the cases in which they were used, and it is possible that the more formidable onlay graft fixed by metal screws has been used in cases in which a simpler procedure would have been successful. On the other hand, when operating for nonunion it is advisable to do a little more, rather than a little less, than will be necessary to secure the desired result, because the patient has already had an unusually long period of disability following his injury.

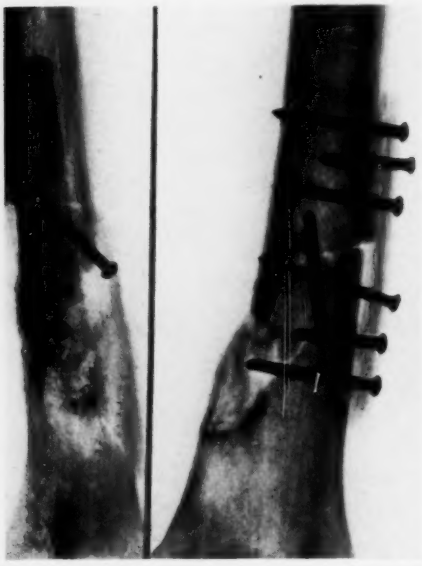

FIG. 11.—Nonunion of the femur treated by an onlay graft, with multiple drilling and accessory bone, and a long oblique screw at right angles to give rigid fixation. Immobilized in a plaster spica for three months.

In nonunion of fractures of both bones of the forearm and other small bones and in fractures near the ends of long bones and of the olecranon, the intramedullary autogenous bone peg is the operation of choice, even though it is condemned by many surgeons. A round hole (¼ of an inch for the radius or ulna) is drilled into the marrow canal of each fragment and a square peg of approximately the same diameter is cut from the tibia and driven tightly into one fragment and then forced by pressure into the other fragment. Then, a small hole is drilled through each fragment (not through the peg) and a loop of stainless steel wire is twisted tightly to pull and hold the fragments together. The failure to use this wire is one cause of failure in this type of graft. Finally, some slivers of bone and bits of cancellous bone are placed around the fracture-line. (Figs. 4 and 5).

I have not used the Albee wedge graft, but have used a massive graft with reduced square ends to fit in round holes to span relatively large defects. This is really a modified medullary peg. Likewise, I have had no experience with the method of Gill, who splits off a massive graft to include about half of the thickness of one fragment and slides it down to bridge the defect and fixes it to the ends of each fragment with metal screws.

Osteoperiosteal grafts, sliver grafts, bone chips and cancellous bone are useful mainly to fill defects and to stimulate osteogenesis at the site of nonunion which is bridged by some other type of graft or a metal plate. I believe that more experience will increase the use of Abbott's iliac grafts combined with bone plates.

After any of the above operations the wound is sprinkled with sulfonamide powder and closed without drainage. The suture line is sprinkled

FIG. 12 FIG. 13

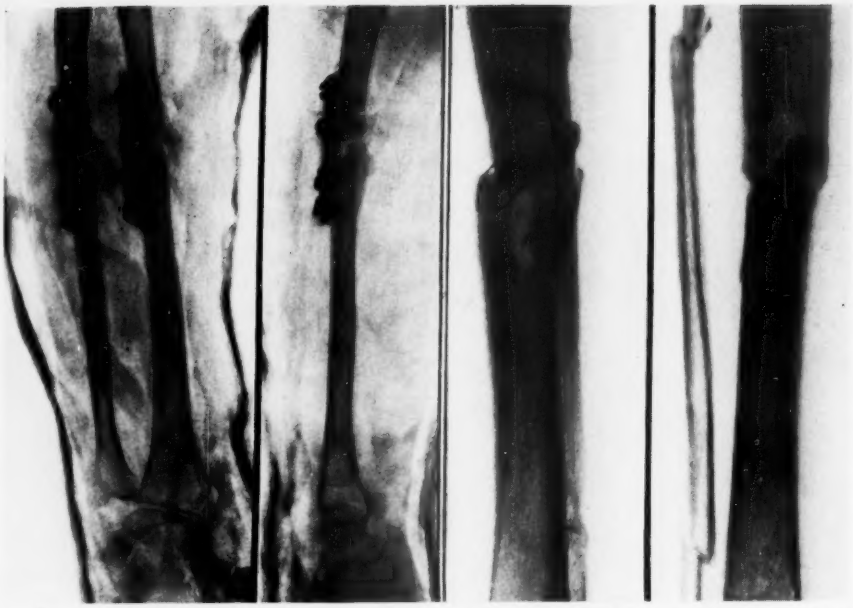

FIG. 12.—Nonunion of forearm of nine months duration, with two previous operations. Treated by onlay grafts, with multiple drilling and accessory bone. Immobilized in a plaster encasement for ten weeks.

FIG. 13.—Old nonunion of the tibia after open reduction and wiring.

FIG. 14 FIG. 15

FIG. 14.—Same after Phemister splint graft, with multiple drilling and accessory bone. The wire was not exposed, but was cut during the drilling. Immobilized in a plaster encasement for ten weeks.

FIG. 15.—Old double fracture, with nonunion of both. Treated by long splint graft fixed by screw to middle and distal fragments. Both fractures were drilled and accessory bone was used. Immobilized in a plaster encasement for eight weeks; then active exercise.

with sulfonamide powder and the limb is immobilized in a plaster encasement applied over a thin dressing and very little padding. This encasement is not intended to allow walking, and it is left on until sufficient time has elapsed for the development of fairly firm union (eight to twelve weeks). The wound is not inspected nor are the skin sutures removed until the encasement is removed. Early change of plaster or the cutting of a window in the plaster may result in angulation of the fragments or even fracture of the graft or loss of position and weight-bearing may disturb immobilization. The patient usually leaves the hospital a few days or a week after the operation and when he returns the encasement and sutures are removed, roentgenograms are taken and the stability is tested and, if necessary, a new encasement is applied for four weeks or more, but this is rarely necessary.

FIG. 16.—Old nonunion of tibia.

CONCLUSIONS

1. With the added insurance against infection provided by the local use of sulfonamide powder in the wounds, operations for the correction of delayed and nonunion of fractures should be performed earlier than in the past.

2. The surgeon should choose an operation which he is able to perform satisfactorily and which can be expected to result in union of the fragments in good position.

3. The simpler procedures are less apt to be followed by postoperative complications than are the more difficult operations, but they will not solve the more difficult problems.

4. A relatively simple operation, if undertaken early, may save the patient time, avoid a difficult late operation, and result in a better limb.

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FIG. 17 FIG. 18

FIG. 17.—Same after multiple drilling, step-cut operation, wire fixation, splint graft and accessory bone. Union after ten weeks fixation in a plaster encasement.

FIG. 18.—Nonunion of tibia fixed by a bone plate and multiple barrel stave grafts of Steel, plus drilling and accessory bone to secure union.

FIG. 19.—Old subtrochanteric fracture which had had three previous operations. Fixed by Neufeld nail and multiple barrel stave grafts, plus drilling and accessory bone used to secure union. Immobilized for four weeks in plaster boots fixed to a crossbar to maintain abduction.

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THYROCARDIAC DISEASE*

A REVIEW OF 614 CASES

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IN THE LAST TWENTY-FIVE YEARS the advances in the surgical treatment of the thyrocardiac and the results of surgery in the patient with hyperthyroidism limited cardiac reserve have been striking and gratifying. These advances fall naturally into five definite periods.

In the first period, approximately twenty-five years ago, many cases of hyperthyroidism with cardiac failure were not even diagnosed. Many times the physician failed to appreciate that the cardiac failure resulted from the associated hyperthyroidism. Most patients with a diagnosis of thyroid disease and associated cardiac failure were rejected as hopelessly inoperable, because the mortality was almost prohibitive.

The second period started a little over twenty years ago when Hamilton,[1] who was then associated with the Lahey Clinic, published his first paper on heart failure and hyperthyroidism. In 1924, Hamilton and one of us (F. H. L.)[2] described the diagnostic difficulties and surgical treatment of these patients and applied to them the term thyrocardiac. In this pioneer era in the management of patients with cardiac decompensation associated with hyperthyroidism, it was demonstrated that these patients could endure subtotal thyroidectomy with a reasonable mortality and that subsequently an extraordinary degree of activity and cardiac capacity were restored and retained.

The third period, in which iodine was popularized by Dr. H. S. Plummer, of the Mayo Clinic, was a most important one in the surgical treatment of hyperthyroidism, since it contributed so materially to reduction of operative mortality.

The fourth period, which may be described as the total ablation period, was advocated by Blumgart, Levine and Berlin.[3] This method has been discarded here and largely elsewhere. The reasons are obvious after a careful study of Figure 1, which shows the relation of the circulation rate to cardiac damage and metabolic rate, and the anticipated results in patients with decompensation without the promoting and removable factor of hyperthyroidism.

The fifth, and present, period is characterized by a much better understanding of what causes decompensation in a patient with hyperthyroidism (Fig. 1); why the patient is so dramatically benefited by subtotal thyroidectomy; and why the benefits of subtotal and total thyroidectomy in a patient

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with decompensation but without hyperthyroidism are so transitory. This period is characterized, further, by an improved understanding of oxygen needs, preoperative preparation, anesthesia selection, postoperative care, and less importantly, vitamins. In spite of these advances, the mortality continues to be high and, we believe, could be lowered.

In the sixth, and future, period, we hope that the diagnosis will be made in the early stages of decompensation and that surgery will be undertaken before decompensation and auricular fibrillation have existed over a long period of time. In this anticipated period, we hope the internist will realize that

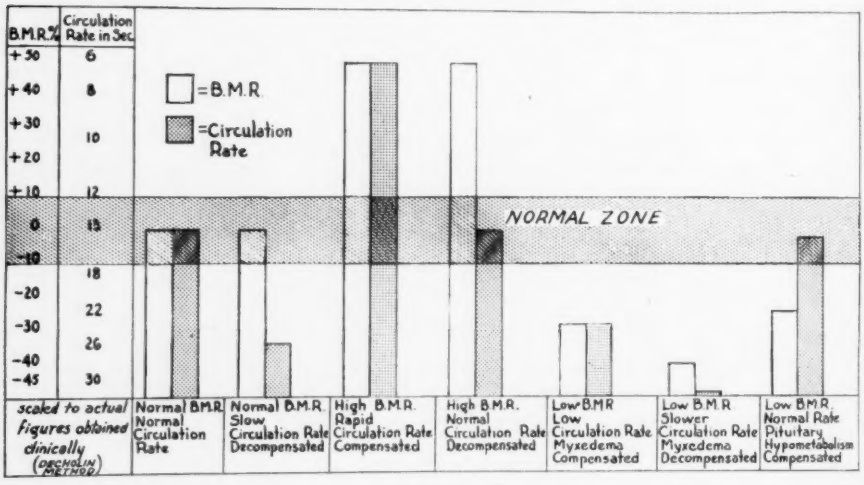

FIG. 1.—Relationship of circulation rate to metabolic rate in various types of thyroid disease and hypometabolism.

cardiac decompensation is found much more frequently in patients with toxic adenoma than in patients with primary hyperthyroidism. We hope the internist will appreciate that while young persons with toxic adenomata, and some limitation of cardiac reserve, frequently fail to show cardiac decompensation, persons past 50 years of age, with the effects of age, effort and disease upon the heart, tend much more frequently to show decompensation. Such is the association of cardiac decompensation with toxic adenoma that in this future era the removal of mildly toxic adenomatous goiters in patients over 50 years of age might reasonably be suggested as a prophylaxis against later cardiac decompensation. We believe that in the presence of auricular fibrillation with hyperthyroidism, immediate surgery is justifiable, in spite of the fact that auricular fibrillation may produce few symptoms. When one realizes that auricular fibrillation and hyperthyroidism are the two most important factors in producing decompensation, that subtotal thyroidectomy will eliminate hyperthyroidism almost at once and will restore normal rhythm in 72 per cent of cases, the prophylactic benefit of prompt surgery with the onset of auricular fibrillation is evident.

WHAT IS A THYROCARDIAC?

The term thyrocardiac has a limited meaning and does not include patients with hyperthyroidism and simple heart disease. Even though the operative risk may be above average, such a patient is not labelled as a thyrocardiac. In our early reports[2] we realized the necessity of defining the term thyrocardiac; first, to avoid misunderstanding as to the type of case, and, secondly, to include only those cases in which the heart complications seemed definitely attributable to the overactive thyroid.

In the great majority of thyrotoxic patients, auricular fibrillation is a manifestation of hyperthyroidism. Congestive heart failure results from excessive thyroid drive on the heart, in most instances with auricular fibrillation but in some instances with regular heart rhythm. The most conclusive reasons for this deduction are that following subtotal thyroidectomy auricular fibrillation usually clears spontaneously and that recurrent congestive heart failure following subtotal thyroidectomy is exceedingly rare without recurrence of hyperthyroidism or severe heart disease unrelated to hyperthyroidism. Thus, a thyrocardiac has a condition precipitated by hyperthyroidism and relieved by cure of the hyperthyroidism.

We wish to emphasize that a true thyrocardiac has clinical hyperthyroidism. This does not mean only an elevated metabolic rate, which may occur in congestive heart failure without hyperthyroidism, nor does it mean a large nontoxic goiter, auricular fibrillation or congestive heart failure resulting from other heart disease without clinical hyperthyroidism. A true thyrocardiac has well-recognized hyperthyroidism, as may be deduced from the history and from the general physical findings. A true thyrocardiac, with few exceptions, has an elevated basal metabolic rate.

A cardiac patient, even one with congestive heart failure, who is operated upon for nontoxic or questionably toxic goiter, apparently may be benefited for a limited time. Generally speaking, if the evidence of hyperthyroidism in a cardiac patient is minimal or questionable, so then is his likelihood of permanent help and sustained restoration of compensation by subtotal thyroidectomy. The enforced rest, the preoperative cardiac care, and the careful postoperative regimen are largely responsible for the improvement following removal of a nontoxic goiter unless the combination of heart disease and a compressed trachea is present. In addition, the frequent production of postoperative thyroid deficiency or myxedema, as was demonstrated in total ablation, lessens the load on the heart only temporarily. Thus, we have not seen permanent relief from subtotal thyroidectomy in patients with goiter and heart disease without hyperthyroidism and do not recognize such an entity as cardiotoxic goiter, as described by Schmidt and Hertzler.[4]

Heart failure in hyperthyroidism is a manifestation of inability of this organ to meet the abnormal demands of an increased metabolism. Heart failure without hyperthyroidism is a manifestation of inability of this organ to meet the usual demands of a normal rate of metabolism (Fig. 1). Thus, the cessation of the abnormal demands of hypermetabolism relieves the unusual

strain on the heart, so that when normal conditions return, the heart is capable of carrying on without difficulty.

In brief summarization:

1. No conclusive evidence exists that hyperthyroidism damages the heart although it may produce physiologic exhaustion.

2. Auricular fibrillation in hyperthyroidism is not in itself evidence of structural damage.

3. Gross cardiac hypertrophy from hyperthyroidism rarely occurs without coincident cardiovascular disease.

4. The large heart shadow in some thyrocardiac patients is the result of dilatation from congestive heart failure and return to normal size may be expected in the majority of patients.[5]

TREATMENT

Preoperative.—The preoperative treatment of the thyrocardiac patient involves two principles:

1. Reduction of the level of metabolism, and thus the work of the heart by (a) rest in bed; (b) adminstration of Lugol's solution; and (c) sedation as needed.

2. Increase in the efficiency of the heart by (a) digitalization if auricular fibrillation is present; (b) removal of the embarrassment of circulation caused by edema, ascites or pleural effusion through the use of salt restriction but not the restriction of fluid, by the use of diuretics, or by paracentesis; (c) venesection and oxygen in rare cases; and (d) an abundant supply of fuel in the form of various carbohydrates, and an adequate nutritional diet including the necessary vitamin factors.

Thyrocardiac patients also require longer preoperative preparation than the ordinary patient with hyperthyroidism. Surgery should not be undertaken too soon, even though some patients may die unoperated. Generally speaking, at least two to three weeks of preoperative treatment are advisable.

Operative.—Because the condition of the thyrocardiac is frequently so desperate and the results of surgery are so dramatic, we assume that no doubt exists, particularly in the minds of those familiar with these cases, that subtotal thyroidectomy is the best and practically the only treatment. The procedure must be a radical subtotal thyroidectomy to avoid a persisting or recurring hyperthyroidism. Unlike the patient with hyperthyroidism only, often the patient has failed to retain compensation in spite of all attempts to limit the hyperthyroidism, short of surgery, and to increase cardiac capacity. Thyroidectomy in the dangerously ill thyrocardiac has a high mortality and consequently must be performed with the aim of preventing even minimal complications.

The patient must be protected against hemorrhage. During the operation this complication interferes with technical accuracy, prolongs the operation, produces shock and promotes anoxemia by depleting the oxygen-bearing blood cells. Postoperatively, this complication involves the hazards of a second operative procedure soon after the first and during a period of reaction.

Tetany has not occurred in any patient in this series, and obviously would be a most undesirable postoperative complication.

As we have already said, perhaps one of the most undesirable complications is the inadequate removal of thyroid tissue, resulting in persistent hyperthyroidism or recurrent hyperthyroidism with the danger of recurrence, decompensation and secondary operation.

To avoid operative and postoperative complications, the surgeon should obtain adequate exposure without reference to the length of the incision. He should keep in mind the ease with which the operation can be performed, and the certainty with which complication can be avoided, and to this purpose, the incision in the skin should be wide, the muscles should be cut, and the lobes should be completely mobilized from their beds. Since as radical removal as

TABLE I

POSTOPERATIVE MORTALITY

Year Group	Number Operated	Percentage Mortality
1922–1931 inclusive	303	4.3
1932–1936 inclusive	170	7.0*
1937–1941	141	11.3
1922–1941	614	6.6

*Erroneously reported as 4.7 per cent of 136 operated cases[6]; actually 7 per cent of 140 operated cases.

possible is desirable, the superior and inferior thyroid arteries on both sides should be tied as a preliminary measure. With wide exposure of the thyroid and a dry field, with accurate demonstration of the nerves, parathyroid glands and the entire thyroid gland, total thyroidectomy can be undertaken expeditiously and with almost complete avoidance of technical difficulties.

While a one-stage subtotal thyroidectomy is desirable in thyrocardiac patients for quick and complete removal of the cause of the decompensation, occasionally because the patient is dangerously ill, a compromise must be made. The cooperative judgment of a surgeon, anesthetist and internist experienced in thyroid disease are of the utmost value. Certain patients will require one-stage, two-stage and occasionally three-stage procedures in order to maintain the mortality rate within limits which are even now undesirably high (Tables I, II and III).

Anesthesia.—An operation upon a thyrocardiac must involve as few operative and postoperative anesthetic complications as possible. The oxygen requirements of the patient with hyperthyroidism during anesthesia are well above those of normal persons, and the maintenance of an adequate supply of oxygen is important. In reviewing our thyroid experiences before employing endotracheal anesthesia to insure unobstructed airways, we were impressed in the thyrocardiac particularly with the fact that prolonged laryngeal spasm or the accumulation of mucus during the recovery period resulted in prolonged and dangerous anoxemia and may have played a rôle in resulting fatalities. Endotracheal anesthesia, as we frequently have observed, is one of the most important contributions to thyroid surgery, especially in the thyrocardiac.

Another important contribution is the aspiration of all mucus from the

TABLE II

NATURE OF POSTOPERATIVE DEATHS

After subtotal thyroidectomy:	
"Storm"	
Age 34, 41	2
After pole ligation only:	
"Storm"	
Age 56, 67	2
After elevation of skin flap only; died on table:	
Previous cerebral embolus	
Age 50	1
Gallop rhythm, history of coronary attack, diabetic:	
Age 70	1
After hemithyroidectomy, preceded by pole ligation four weeks previously:	
"Storm"	
Age 69	1
After second hemithyroidectomy, preceded by two pole ligations and hemithyroidectomy four to six weeks previously:	
"Storm"	
Age 78	1
After hemithyroidectomy:	
Pulmonary embolism	
Age 58	1
Cerebral and peripheral emboli:	
Age 62	1
Probable cerebral embolus:	
Age 64	1
"Storm"	
Age 40, 57, 63, 63, 70	5
Total	16

TABLE III

TYPE OF OPERATION AND POSTOPERATIVE DEATHS

Operation*			
Number	Type	Percentage	Deaths
56	One-stage	40	3
63	Two-stage	44	8
20	Three-stage	15	4
2	Four-stage	1	1

*Type of operation planned and carried out unless death occurred before all procedures were performed.

trachea just before removal of the intratracheal catheter, thus, often preventing tracheal obstruction and resulting anoxemia which occurs during recovery from anesthesia before the patient regains the ability to eject spontaneously the accumulated mucus in his bronchi.

No factor is more important in operative mortality in the thyrocardiac than the selection of the proper anesthetic agent. In the period before the present one, we enthusiastically advocated the use of cyclopropane, particularly because of the high percentage of oxygen in a cyclopropane mixture. However, we have had three operative deaths in thyrocardiacs from probable ventricular fibrillation promoted by cyclopropane. One of these deaths was literally heard in the stethoscope while the anesthetist was taking the blood pressure, that is, sudden and complete cessation of all pulse sounds. We now employ cyclopropane in thyroid patients, and particularly thyrocardiacs, only as an induction agent and then only in mixtures not exceeding ten per cent. Ethylene, without the tendency to produce cardiac irregularities, is a satisfac-

tory induction agent for the thyrocardiac. As a result of these experiences with ethylene and cyclopropane, and following the published[7] laboratory data on the effect of cyclopropane upon the epinephrine sensitized heart, cyclopropane has now been largely abandoned in favor of ethylene supplemented with ether. We now realize that in giving cyclopropane to a thyrocardiac we were superimposing another cardiac irritant upon a heart muscle already suffering from a cardiac irritant—thyroxin.

The physician is apt to think that the thyrocardiac, often having had associated ascites, edema, orthopnea and cardiac irregularities, is too ill for inhalation anesthesia. Because of this and because the patient is awake and is not inhaling an anesthetic agent, he easily can be misled into believing that local anesthesia is safer. However, with a proper inhalation anesthetic and an intratracheal catheter in place, the patient may often be breathing a richer mixture of oxygen than when under local anesthesia.

The two most advantageous features of an inhalation anesthetic are (1) the employment of an intratracheal tube or airway, thus supplying an adequate and constant supply of oxygen; and (2) the production of definite relaxation with a good supply of oxygen and as little irritation to the heart muscle as possible.

For the thyroid patient, and specifically for the thyrocardiac, local anesthesia has not only no advantages but many disadvantages. The disadvantage for the patient is the creation of undesirable emotional and psychic states, and the disadvantages for the surgeon are that it fails to permit adequate exposure, a dry field and a clean-cut anatomic dissection. In addition, a longer period of time is necessary to perform the operation.

Avertin, while attractive from both the patient's and surgeon's point of view in permitting transportation of the patient to and from the operating room while asleep, is an undesirable anesthetic agent for the patient with hyperthyroidism and particularly for the thyrocardiac. It is followed by a long period of postoperative depression, with accumulation of bronchial secretion, and sometimes with the undesirable complication of an inadequate supply of oxygen.

After a number of years of combined effort by the surgeon, anesthetist and cardiologist, we have concluded that ether is the safest and most satisfactory anesthetic agent for the thyrocardiac. This is a radical change of viewpoint from some of our previously expressed opinions, and certain qualifications concerning the use of ether are necessary. We are strongly opposed to ether as an induction agent, since it promotes psychic stimulation, agitation and struggling, and requires a long time. The safest anesthetic procedure for the thyrocardiac is to give 1.5 grains of pentobarbital sodium the night before operation and ⅙ grain of morphine and 1/150 grain of scopolamine one and one-half hours before operation, followed by 1.5 grains of pentobarbital sodium one hour before operation, and then induce anesthesia with ethylene and continue with ether.

Postoperative.—All patients with hyperthyroidism, with or without car-

diac damage, are placed in oxygen tents postoperatively to facilitate breathing, and particularly in thyrocardiacs, to lighten the load upon the heart. Saklad[8] called attention recently to the necessity of tents that do not leak, and the frequent testing of content to be certain that the oxygen percentage is being maintained at the desired level. As he pointed out, because of lack of supervision many patients undoubtedly never receive an adequate percentage-mixture of oxygen.

Thyrocardiacs, as well as all other patients operated upon for hyperthyroidism, receive an intravenous glucose solution postoperatively. One must be careful, however, lest cardiac embarrassment results from too enthusiastic employment of this useful measure. Intravenous glucose in five

TABLE IV

PERCENTAGE OF AURICULAR FIBRILLATION PERSISTING TO DATE IN OPERATED PATIENTS

Year Group	Percentage
1922–1931 inclusive	27
1932–1936 inclusive	28
1937–1941 inclusive	26

Normal Rhythm	Persistent Auricular Fibrillation	Percentage Auricular Fibrillation
222	84	27

per cent solution may be given in quantities not exceeding 2,000 cc. in 24 hours. With the increase in metabolism following operation, the body can easily handle this quantity in addition to that taken by mouth. The cardiac burden will not be increased if the solution is given slowly, at least two hours being taken for the introduction of each liter of fluid.

Iodine is administered in intravenous solution at the rate of 30 minims in 24 hours. Morphine in liberal amounts to reduce restlessness is desirable, but care must be taken not to overdo the use of this valuable drug, thus completely suppressing the cough reflex and inducing the extremely dangerous postoperative complication of pneumonia.

For two or three days postoperatively the patient accumulates a good deal of mucus as a result of secondary tracheitis, and is in constant danger of partial or complete unilateral atelectasis. The mucus should be aspirated from the trachea with a rubber catheter when atelectasis has not taken place and bronchoscopy should be undertaken promptly, under local anesthesia, when partial or complete unilateral atelectasis has occurred. We have seen dramatic results follow suction bronchoscopy in thyrocardiacs with atelectasis following the removal of mucus from the bronchi and aeration of the atelectatic area.

Preoperative and Postoperative Quinidine Therapy.—Quinidine should not be employed in thyrocardiacs until after the completion of all operative procedures. If it is used preoperatively to stop auricular fibrillation the irregularity almost certainly will return postoperatively.

While the majority of patients with auricular fibrillation have a return of normal cardiac rhythm within the first few months after operation, it can be

restored more quickly by the use of this drug if given a week or so after the final operative procedure. We have not employed quinidine sulfate as much during the last five years as formerly, yet the percentage of persistent auricular fibrillation has remained fairly constant (Table IV). This would suggest that while quinidine postoperatively promptly restores normal rhythm, in most instances normal rhythm would have occurred spontaneously later.

On the basis of this experience, the value of quinidine sulfate for the thyrocardiac can be questioned. Since the drug is toxic, and must be given with caution, we doubt whether its use is as advisable as we formerly believed. The fear of embolus following its use is its chief drawback, but, in our experience, this has occurred but once.

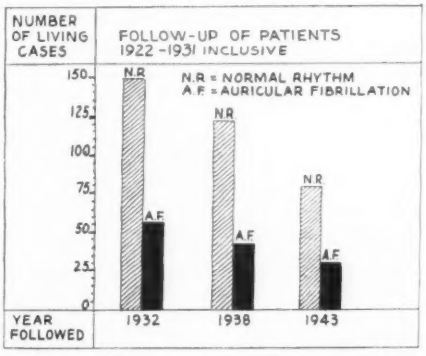

FIG. 2.—Ratio of persistent auricular fibrillation to normal rhythm in surviving patients operated upon between 1922 and 1931. Persistent auricular fibrillation does not increase death rate.

In spite of apparent subsequent embolic deaths in these cases, auricular fibrillation is probably no greater hazard than normal rhythm as far as life expectancy is concerned since death has occurred as frequently in the group of patients with normal rhythm as in those with auricular fibrillation (Fig. 2).

FOLLOW-UP STUDIES

Another follow-up of all thyrocardiacs recently was completed (Table V). This study was chiefly by questionnaire, many of which were completed by the patient's physician. Evaluation of the present results was established as follows:

Grade 1: Patients able to carry on normal activities commensurate with individual age, with no myxedema, regular heart rhythm and no recurrence of hyperthyroidism.

Grade 2: Patients still having auricular fibrillation or postoperative myxedema requiring thyroid, or having had a recurrence of hyperthyroidism controlled by iodine, who carry on normal activities.

Grade 3: Patients incapacitated by any complication attributable to their thyrocardiac condition such as hemiplegia from embolus, incapacitating recurrence of hyperthyroidism, or congestive heart failure without hyperthyroidism.

TABLE V

PRESENT STATUS OF 614 OPERATED THYROCARDIACS*
1922–1941, Inclusive

Year Group	Percentage Alive	Percentage Dead
1922–1931 inclusive	35	32
1932–1936 inclusive	54	24
1937–1941 inclusive	75	18
Known alive		306
Grade 1, 201		
Grade 2, 100		
Grade 3, 5		
Known dead		165
Untraced		143
Incidence of postoperative myxedema		2.9%
Incidence of diabetes		3.6%

*At operation, 60 per cent over 50 years of age.

We realize that patients may not always know whether the pulse is regular or irregular. If auricular fibrillation was shown by the record to have existed a year or more after operation, and the patient reported irregularity, the condition was assumed to continue even when the rhythm was normal on last examination. The patient with probable auricular fibrillation was graded 2. Because of the improbability of a recurrence of auricular fibrillation without recurrence of hyperthyroidism, these patients were asked to return for reexamination; however, only a few patients made such a report. Thus, in reporting the presence of auricular fibrillation, we have erred on the side of a greater number having this irregularity than not having it.

TABLE VI

THYROCARDIAC CASES
1937–1941, Inclusive

Total number seen	147
Operated	141
Postoperative deaths	16
Died, no operation	4
Refused operation	2
Preoperative cardiac status in operated patients:	
Congestive heart failure with regular rhythm	10
Congestive heart failure with auricular fibrillation	56
Established auricular fibrillation without congestive heart failure	75
Total	141

A new group of thyrocardiacs, those patients operated upon from 1937 to 1941 inclusive, is reported (Table VI). In this group of patients, followed from one to five years, the results are essentially the same as in the other groups followed for the same length of time.

SUMMARY

The name thyrocardiac, applied by one of us (F. H. L.[2]) to this condition in 1924, called attention to this interesting group of patients in whom early diagnosis and early subtotal thyroidectomy can accomplish such gratifying restoration of cardiac capacity and physical activity.

The present is the fifth period, so to speak, in the treatment of this condition. A sixth period is hoped for, in which earlier diagnosis and operation,

and even prophylactic subtotal thyroidectomy for early toxic adenomata and early auricular fibrillation would give even better results.

The necessity in speaking of a thyrocardiac as one having indisputable hyperthyroidism is stressed. The reason the true thyrocardiac permanently regains cardiac compensation after subtotal thyroidectomy and the false thyrocardiac does not, is discussed under the heading "What Is a Thyrocardiac?"

The preoperative and operative management is discussed, as well as postoperative care and preoperative and postoperative employment of quinidine.

The results of our experience with various types of anesthesia are discussed, and a conclusion reached as to the best combination of narcotics and anesthetic agents for the thyrocardiac.

The end-results in 614 cases, from 1923 to 1933, and from 1933 to 1943, are presented.

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DISCUSSION.—DR. ROBERT S. DINSMORE (Cleveland): Doctor Lahey always presents material which is of prime clinical importance. The question of auricular fibrillation is extremely important in this group of cases as a whole, and I am sure that the incidence is much higher than is generally supposed.

In an analysis of 1000 consecutive patients with hyperthyroidism in our series, Ernstene found that 20.7 per cent had auricular fibrillation in one of three forms. It had occurred, first, as a paroxysm of fibrillation preoperatively; secondly, in the continuous form; and, thirdly, postoperatively, without evidence of congestive heat failure.

These figures vary slightly from Doctor Lahey's because if one takes these cases as a whole it is found that in the 20 per cent, about half of them have either an associated arteriosclerosis, a hypertensive disease, or an organic heart lesion.

In spite of bed rest, Lugol's, digitalis, and sedatives, we find nine per cent of these patients fibrillate preoperatively, and 11 per cent postoperatively. I have felt that this postoperative incidence was too high, and if there were some criteria whereby we could increase the number of patients who were digitalized before the operation, this postoperative incidence could be lowered. The present criteria for the cardiologist

in administering digitalis are: First, that the patient have auricular fibrillation; or second, evidence of congestive heart failure. In our cases, four per cent had congestive heart failure, nine per cent fibrillated before the operation, so at most 13 per cent were digitalized preoperatively.

The reason I have felt so strongly about this is because I saw a large series of cases during 1921–22 on Doctor Crile's service at Lakeside Hospital, in which the bane of our existence was the incidence of postoperative auricular fibrillation and the casualties that went with it. This was before the days of Lugol's solution and Doctor Plummer's advice about that, so we started a large series of cases in which we routinely digitalized, and we were amazed to find a very marked drop in the incidence of postoperative auricular fibrillation.

Some believe a postoperative auricular fibrillation is not of much significance, but I think, as Doctor Lahey has emphasized, that it is a danger signal. It is not only a danger signal from the two points he has mentioned—namely, the possibility of congestive failure or the possibility of emboli—but also I have seen the onset of a postoperative auricular fibrillation be the initial sign in a long and stormy convalescence, particularly in the elderly patient who develops this arrhythmia, edema and bronchitis, and occasionally bronchopneumonia. In spite of chemotherapy we still have occasional deaths in this group.

On the question of angina with regard to the thyroid, I thoroughly agree with Doctor Lahey, with regard to total ablation and in our hands it has been absolutely ineffectual. I have discarded the procedure as far as I can, and I have no confidence whatsoever in the operation. I have thought the best result I had was in a man who had had anginal symptoms. I removed the thyroid. He was very much elated about the result because instead of being able to walk one block he was able to walk two blocks without pain. However, a short time after that he died with a typical coronary episode. That is about our experience with these cases. I am quite sure that Colonel Claude Beck has made a more rational suggestion in handling anginal cases than anything the thyroid surgeon has to offer.

I also want to give a note of warning about the use of quinidine. We use it a little differently than Doctor Lahey does. We have chosen the seventh postoperative day for its use in the patient who has had continuous fibrillation. We do this because it is about the end of the hospital stay, and we like to give them the quinidine while they are in the hospital in bed. We start them on three grains four times a day, or 0.2 Gm., and continue it until a normal rhythm is restored, and something over half of these cases have reverted to a normal rhythm.

I want again to warn that the housemen, or whoever is responsible for the administration of the quinidine, know the four contraindications for its use: First of all, be sure that this patient has had no history of previous embolic accident; that the heart is not enlarged; that he has no associated organic heart disease; and, above all, that he has no idiosyncrasies for the drug.

I have had a little different experience with avertin than has Doctor Lahey. I personally have used it over a ten-year period in thyroid work. I agree with him that it has a full anesthetic effect, and that it is a bad anesthetic particularly in elderly patients, since they do get a marked cerebral depression; for this reason I do not like it for these cases. I have used it in conjunction with local anesthesia, however, and the ordinary case receives from 65 to 70 mg. per kilo of body weight. These patients are really drowsy, but they can be aroused at any time, and in conjunction with local anesthesia it has been entirely satisfactory in my hands. It is an ideal anesthetic for the very young child, three, four or five years of age, with a severe exophthalmic goiter.

Again I want to repeat, as Doctor Lahey has stated, that it is a great satisfaction and gratification to have one of these desperately ill patients with a congestive heart failure, following a slow, unhurried preparation, have no postoperative cardiac complications following thyroidectomy.

DR. FRANK H. LAHEY (Boston, closing): To avoid confusion in the results of treatment, it is important that we all have the same understanding of the term "thyrocardiac."

A patient with hyperthyroidism and a compensated cardiac lesion is not a thyrocardiac.

A patient without hyperthyroidism and with a large nontoxic goiter and a cardiac condition is not a thyrocardiac. A true thyrocardiac is a patient with hyperthyroidism and resulting cardiac failure. That does not mean even that a patient with an increased basal metabolism and an enlarged thyroid gland who has cardiac decompensation is a thyrocardiac.

Unfortunately, we still have to use our senses in clinical and laboratory diagnosis. A patient, particularly with the hypertensive type of cardiac failure, can have an increase in metabolism up to +40 per cent. To establish the diagnosis that a patient is a thyrocardiac, one needs clinical evidence of hyperthyroidism, an increase in basal metabolism as a result of hyperthyroidism, and cardiac failure as a result of the circulation rate caused by the hyperthyroidism.

There are a few other things which I should like to mention. Is there such a condition as a true thyroid heart? There has never been any convincing evidence, microscopic or otherwise, that hyperthyroidism by its direct effect upon heart muscle produces damage. Auricular fibrillation does produce a rhythm which in the overburdened heart of hyperthyroidism tends to produce failure, but concerning that I can only say that auricular fibrillation frequently is associated with hyperthyroidism and is not, in itself, necessarily evidence of heart damage from thyroid intoxication.

We repeatedly have stressed the importance of keeping this group of cases in mind to avoid overlooking them, particularly because the urgency of the decompensation in the apathetic type of hyperthyroidism so often associated in the elderly with decompensation and hyperthyroidism, confuses the picture and makes the diagnosis difficult. Diagnosis is important, as evidenced by our end-result figures, because there is an excellent opportunity to restore these patients dramatically to long-continued and useful activity.

SKIN REMOVAL IN RADICAL BREAST AMPUTATION*

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Most of the debatable questions concerning cancer of the breast have been answered by carefully prepared statistics of postoperative results. Nearly fifty years have elapsed since Halsted published his first paper, in 1894, based on the first fifty cases operated by his method from which all modern operative procedures spring. Many have contributed to it since then. It is not, therefore, the object of this paper to reemphasize facts generally accepted.

Lewis and Rienhoff's paper, published in the Annals of Surgery, in March, 1932, covered in detail the statistical data of the results of the operative treatment of cancer of the breast at the Johns Hopkins Hospital from 1889 to 1931. This paper was based on 950 cases, 750 of which were operated upon by 38 different surgeons. Haagensen and Stout, in the Annals of Surgery for December, 1942, have added an excellent statistical study of 1040 cases observed from 1915 to 1934, 640 of whom had radical mastectomies. These operations were performed by 36 different surgeons at the Columbia Medical Center in New York City. In these two papers particularly, those interested will find many important problems discussed and answered by statistical data.

There are, however, still a few questions apparently unsettled—one of these, the oldest of all in radical breast surgery, is the question of skin removal. This question is important since it inevitably leads to the other problems still debatable—local recurrences and the necessity of skin grafting. In a paper read before this Association last year, William C. White, of New York, reported 238 cases operated upon by him and other members of the Staff of the Roosevelt Hospital. He expressed a preference for the Handley technic, and gave the impression that wide skin removal was secondary in importance to fascial removal. In this group, however, there were 22.6 per cent of local skin recurrences, while in the larger group studies by Lewis and Rienhoff there were 19.2 per cent local recurrences, and in the group studied by Haagensen and Stout, the statement is made that "the incidence of local recurrence in the operative field continues to be distressingly high—22.8 per cent of those surviving five years."

A special interest in this subject, now for the past 35 years, in the first eight of which I had the opportunity of assisting my father, had led to certain firm convictions on these still debatable questions which are:

First, that wide skin removal is important since, in our opinion, it must be the chief reason for local recurrences when insufficient skin is removed.

Second, that by combining wide skin and fascial removal such recurrences can all but be eliminated.

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

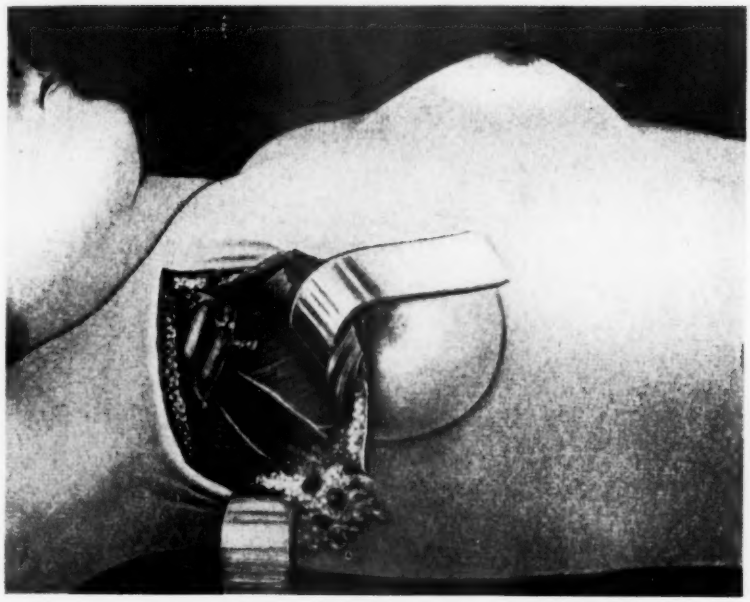


FIG. 1.—Axilla dissected first. Straight incision on chest wall beginning 1 inch below clavicle 2 fingers' breadth from edge of shoulder extending downward 4 or 5 inches through skin and subcutaneous fat—Pectoral portion of pectoralis major and tendon of pectoralis minor divided at their insertions. Axillary node tearing fat and fascia dissected from above downward. Vessels ligated at source of origin. Subscapular nerve on posterior wall and long thoracic (external respiratory nerve) on inner wall preserved.

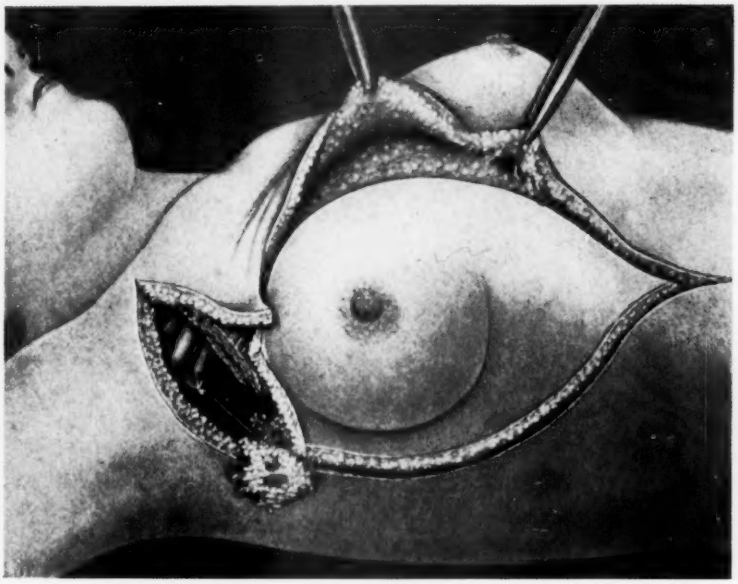


FIG. 2.—Egg-shaped incision around breast and well down on to upper rectus. Large amount of skin removed. Extensive undermining of skin begun. At no point should edge of skin remaining have been closer than 2 inches to edge of growth.

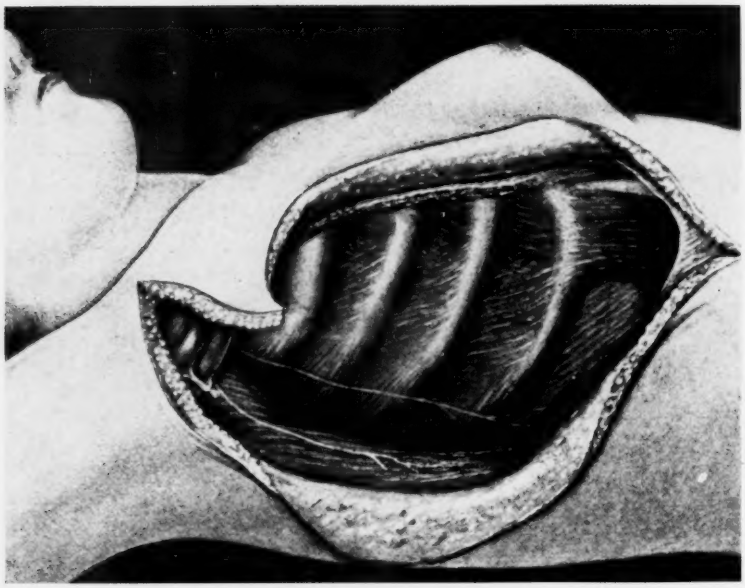


FIG. 3.—Entire breast with overlying skin and underlying pectoral muscles with axillary nodes and upper pectoral fascia on affected side removed. Undermining of skin carried over to midsternal line in front and to edge of trapezius behind.

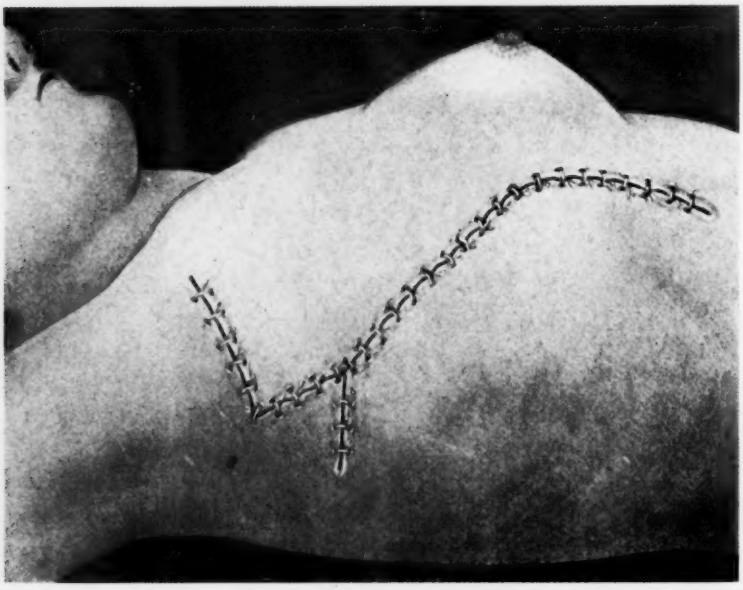


FIG. 4.—Wound closed—drain to axilla—extensive undermining makes grafting unnecessary.

FIGS. 5 and 6.—A comparison of specimen as removed by Handley method (Fig. 5 top) and by Rodman method (Fig. 6 bottom). Note much greater amount of skin removed by Rodman method.

Third, that with a properly planned procedure skin grafting is unnecessary except in the rarest instances.

Fourth, that with such a procedure the usefulness of the arm on the operated side should not be impaired.

Any operative method which should merit continued use must combine the steps in technic made necessary by the work of those who have given sound reason for them. We all accept as fundamental the work of Halsted and Handley, particularly. If the principles brought out by these and others can be combined into one procedure and if such a procedure can show as large a percentage of cures and eliminate certain undesirable sequelae it would seem that it should merit continued use.

W. L. Rodman, in 1908, first advocated a method of radical breast amputation which he believed would meet these requirements. I believe that the method has more nearly done so than the original Halsted or Handley technics and that, therefore, it has deserved a greater usefulness than it apparently has had.

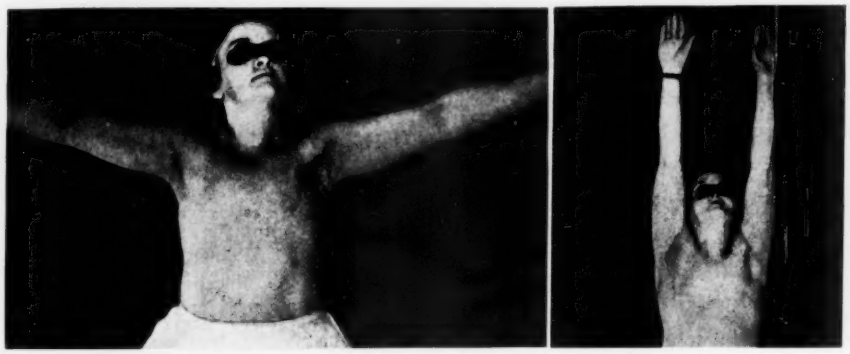
Some 65 years ago, the younger Gross (Samuel W.), was the first to show that wide skin removal was the first important step that should be made a part of the technic of breast amputation. At that time, D. Hayes Agnew, then Professor of Surgery at the University of Pennsylvania, remarked toward the close of his surgical career that he "had removed a cartload of breasts and never cured a case." Gross claimed that he was saving 9.5 per cent of his cases for three years.

They both were amputating the breast only, Agnew through the small elliptical incision, which removed a very small amount of skin, and Gross, using his "dinner plate" incision, removed all of the skin overlying the breast itself, allowing his wounds to granulate. It is interesting to see how each step added since then to the modern procedure resulted in definite improvement in results. Gross, continuing his interest, added an axillary dissection, or at least what he thought was one, by extending from the top of his incision, a straight one to the axilla. The muscles were not removed and we know that, anatomically, it was impossible for him to have removed any more than the lowermost group of lymph nodes and fat at the base of the axilla. Nevertheless, his three-year cures were more than doubled—21.5 per cent. Sir Mitchell Banks, performing the same operation, had the same results—21 per cent. Bull, of New York, performed a more thorough axillary dissection and had slightly better results—26.6 per cent three-year cures. In 1894, Halsted published his study of 50 cases, the first to be undertaken by the procedure which became a classic and which today is essentially the one most widely followed—at least in this country;—38.3 per cent were free from recurrence or known metastasis after three years.

In 1906, Handley published the first edition of his monograph on Cancer of the Breast. In a 2nd edition, published in 1922, he states that of 31 cases operated upon by his method, 48 per cent survived the three-year limit. In 1915, W. L. Rodman published the results of the first 50 cases operated

upon by his method. Of these, 72 per cent were well for three years and 24, or 48 per cent, for five years.

This method has been fully described elsewhere, and the details of the technic need not be gone into here. (W. L. Rodman's Monograph on Diseases of the Breast: With Special Reference to Cancer—1908. A Lecture on Cancer of the Breast. Murphy's Clinic, Vol. IV, April, 1915). Suffice it to say that it has proven so satisfactory, over the years, that no changes have seemed necessary to add to it. As stated at the beginning of this paper, it is not our object to reemphasize all of the many accepted facts now amply proven by statistics and generally accepted. In reviewing many of the papers on this subject, I have been impressed, however, with the fact that from



FIGS. 7 and 8.—Showing usefulness of arms in a bilateral amputation. Scar does not touch arm, entirely on chest wall. No restriction of motion in abduction of full extension.

large clinics from which have come the most detailed and valuable statistics, these are based on the collected experiences of many operators, some of whom have been experienced, while others have added but a few cases to the study as a whole. This is true of both of the large series statistically studied and referred to in the beginning of this paper. In Haagensen and Stout's series only one of 36 operators had a sufficient number of cases to be of any statistical value. In the 35 years elapsing since the Rodman method was advocated, I am safe in saying that several hundred cases have been operated upon by this method by a small staff, the vast majority by either the originator of the method or myself at our clinic. I am prevented from giving a complete report of the results including private and ward cases by reason of the fact that many of the ward records were lost on moving them twice when the hospital was moved.

Even in the private records, some have proven impossible to trace and, therefore, could not be included in this study. I have been able, however, to trace 132 private cases, all operated upon by W. L. Rodman or myself:

61% have been free from all evidence of recurrence for 3 years
46% " " " " " " " " " 5 years
39% " " " " " " " " " 5–10 years
16% " " " " " " " " " 10–15 years
6% " " " " " " " " " over 15 years

It has been our experience that the first two years is the critical period, and that very few died after five years (of cancer). Fifty-three-plus per cent had axillary metastasis at the time of operation—46 per cent did not Of those with axillary metastasis, 23.5 per cent survived five years or more. Of those without axillary metastasis, 63.5 per cent survived five years or more. A 46 to 48 per cent five-year survival, without any evidence of recurrence, local or distant, compares favorably with any statistics known to me (48 per cent W. L. Rodman, in 1915—and 46 per cent reported in this paper).

To finish this communication where we began, however, I repeat that a procedure yielding the statistics quoted is in general a more satisfactory procedure than others if, in addition, it eliminates certain undesirable sequelae. In the 132 cases reported, a careful check of the records of those known dead and of the surviving patients themselves, have shown only three instances of local recurrence, or 2.2 per cent. This method, therefore, all but eliminates local recurrences which, if they occur early must mean insufficient skin or fascial removal. As stated, White, in his paper of last year, reported 22.6 per cent local recurrences in the Roosevelt series (Handley method)—Lewis and Rienhoff 19.2 per cent local recurrences (Halsted method), Haagensen and Stout 22.8 per cent. Since 1908, not a single case has been skin grafted in our clinic. In a few cases we have had a small part of the center of the wound slough. In none of these has it been necessary to graft. The original Halsted technic calls for skin grafting in the majority of cases, and I understand that this step is still almost the rule at the Johns Hopkins Hospital where the Halsted technic is still largely followed. White reported 17 cases grafted in addition to the 238 cases closed by the Handley technic. If this tremendous wound can be closed, not by a plastic procedure planned before the necessary radical steps are completed, the result is unquestionably better in that a pliable scar, not attached to the underlying chest wall, results. More important than this, is the future usefulness of the arm on the operated side. In scars resulting from the Halsted technic which I have seen, there is always a bridge of scar tissue from the chest to the arm, which results in distinct limitation of motion in abduction and extension. This certainly undesirable sequela is unnecessary and should not be allowed to occur. In our cases, the only limitation of arm motion is seen in the few instances which have developed marked edema. Just why this happens, now and then, is another problem still not adequately explained. We are, of course, quite used to seeing transient and slight edema of the arm due, we suppose, to the lymphatic block. When this becomes persistent, and marked, it may be due to this factor plus a mild type of infection resulting in scar tissue, as suggested by Halsted. We make no effort to confine the arm after 48 hours and, in fact, encourage its use as the scar does not touch the arm and, therefore, is not in any way damaged when the arm is moved.

No communication on this subject should be closed without paying tribute to the excellent work of others who have been especially interested

in it in recent years. Auchincloss, of the Medical Center in New York, and Judd and Harrington, of the Mayo Clinic, particularly, have added valuable studies to it.

CONCLUSIONS

1. Wide skin removal is important.

2. That local recurrences are, at best, undesirable if they do not actually represent an inadequate eradication of the disease and certain of its known zones of local spread.

3. That such local recurrences need not occur except in a very small percentage of cases (2.2 per cent with the method reported).

4. That skin grafting is unnecessary except in rare instances (none since 1908) by the method reported.

5. That arm usefulness should not be impaired as a general rule and never unless marked edema follows.

6. That a method advocated by W. L. Rodman, in 1908, meets these requirements, in addition to saving 46 per cent for five years from recurrence either local or distant, so far as could be demonstrated.

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DISCUSSION.—DR. DONALD GUTHRIE (Sayre, Pa.): I agree heartily with the points brought out by Doctor Rodman. As a matter of fact, I was one of the early enthusiasts of his father's operation, reporting it in 1914. We have used no other type of operation in our clinic since that time.

We believe that wide skin removal, with wide superficial and deep fascia removal are important and essential, for we are sure that skin recurrences come from the fascia underneath the skin and not from the skin itself. Our percentage of skin metastases has been very low, and it has been surprising how long some of these patients will live if these small skin metastases are removed, as they appear. As a matter of fact, I had one patient who lived nine years after the first appearance of metastasis, and who finally died of an hemiplegia. In our meager experience with this condition, the deeper metastases, through the lymphatic and vascular system, have not taken place.

It is surprising to me that these splendid principles embodied in Doctor Rodman's essay have not received more general wide adoption. For instance, the primary axillary section has so many points in its favor. We work from a clean into an involved area, the breast is handled far less than it is in any attack that centers itself upon the breast itself. The blood supply to the breast and to the muscles at the point of origin is controlled, and these operations are far less bloody than the usual operation which attacks the breast first.

Sometimes the condition of the axilla is found to be such that the operation had best be suspended. This was found in thirty of our patients upon primary axillary exploration.

Keeping the scar from the arm is also a most important thing, as is the anatomical, gentle, sharp dissection of the axilla. I am sure that some of the elephantiasis that occurs is due to a mild infection of the axilla which happens almost immediately postoperatively, and it is a factor in interrupting the return of the superficial lymphatics from the arm to the chest wall.

As I said, our number of metastases in the skin have been very small and, while we practice wide skin removal with fascial removal, it has been necessary to skin-graft but few of our cases.

Not to repeat any of the points brought out by Doctor Rodman, I would, however, like to call your attention to the extent of the skin incision, which includes the breast completely and is extended down on the abdomen so that the fascia of the recti can be removed. In the complete dissection with wide skin removal and wide fascia removal as well, the only two structures which are saved are the long respiratory and the subscapularis nerves.

In closing the wound in the center, it is important to use the tension approximation sutures, the far and near, we used to call it. We have found that an important factor in preventing loss of flaps is the "pie-crusting" of the skin, as first suggested by Charles Mayo years ago, to allow an immediate release of serum. If nonabsorbable sutures, either silk or cotton, are used and pressure is placed upon the main wound by a long commercial rubber sponge and another smaller rubber sponge is placed in the axilla, with the wound bound up tightly for four days, we practically have no serum collections of any kind. We have used cotton, with great enthusiasm, in almost all of our work.

The arm is mobilized quickly after the operation and this, I believe, is also a factor in preventing postoperative edema.

In following 409 of our 642 cases carefully, our figures agreed with those of Harrington, in that of those living five years, with no involvement of the axilla, there were 65.5 per cent; living ten years, there were 40.9 per cent. With axillary involvement, at the end of five years there were 23 per cent alive, and at the end of ten years but 9.8 per cent were alive,

It is my belief that the reporting of a group of breast cases without separating those with axillary involvement and those with no axillary involvement at the time of operation leads us into a realm of false security.

DR. J. SHELTON HORSLEY (Richmond, Va.): For many years I have been using the principle of the Rodman operation for cancer of the breast. It is a very satisfactory procedure, and usually the wound can be closed without skin grafting. It is important, of course, as Sampson Handley demonstrated many years ago, that the subcuticular tissue be removed in the block dissection and that but little subcutaneous fat and fascia be left in the adjacent flaps. Handley has shown that cancer spreads in a radiating manner in the subcutaneous tissue as well as through the main lymphatic trunks.

In addition, however, to the local precautions against recurrence, for the last five years I have been removing both ovaries at the time of operation when the patient was within the menstrual age. It occurred to me, partly because of such work as that of Lett, Beatson, and others, who performed oophorectomy in advanced cases of cancer of the breast with some apparent benefit, and also from beneficial results occasionally obtained by roentgenotherapy of the ovaries in cases of cancer of the breast, and the lowered incidence of cancer of the breast in mice after bilateral oophorectomy, that removal of both ovaries at the time of a radical operation for cancer of the breast would increase the cures. Since a large amount of estrogen appears to promote cancer of the breast, it would seem that elimination of the supply at the time of operation would give optimum results in preventing recurrence. Since beginning this procedure on November 19, 1937, up to January 1, 1942, I have performed 12 operations for cancer of the breast accompanied by removal of the ovaries in premenopausal women. Of the 12 cases, 11 were without recurrence at the last follow-up record in September, 1942. One died six months after operation from metastases to the lung and skin. These 11 cases have not, of course, gone through the five-year period, but the results are strongly suggestive. As a rule, in my experience most of the cases of cancer of the breast that recur, do so in the first 18 months after operation.

Huggins in his remarkable work on cancer of the prostate, has shown that roentgenotherapy of the testicles is not as efficient as excision and that the interstitial cells are not permanently destroyed by the roentgen ray. It would seem that this would apply particularly to the ovaries, because they are less exposed and more difficult to destroy by roentgenotherapy.

Three of the earlier patients, Mrs. C. D. A., Mrs. R. P. H., and Mrs. A. D. W.,

are cases with rather high-grade cancer. In one instance (Mrs. C. D. A.) the breast had been removed elsewhere, and there were metastases in the axillary lymph nodes. A radical operation was performed. (Photomicrographs from these three patients shown.)

DR. STUART WILLIAM HARRINGTON (Rochester, Minn.): I wish to congratulate Doctor Rodman on his presentation of skin removal in radical breast amputations and, also, on the excellent results he has obtained from the operative procedure. This is the lowest percentage of local recurrences that I have seen reported.

In the last review of cases which we have studied, our percentage of skin recurrence was approximately eight per cent. There are many factors which enter not only into the percentage of patients having skin recurrence but also into the prognosis as to life for patients who are operated upon for carcinoma of the breast, the most important of which are the extent of the disease at the time of operation and the type and grade of malignancy which are present.

Most surgeons have accepted radical mastectomy as the operative procedure to be utilized for carcinoma of the breast. The greatest variation in technical procedures has been in the type of incision to be utilized. This is important from the standpoint of local recurrence. I believe that the type of incision to be utilized must depend on the location of the growth in the different quadrants of the breast and also the type of breast, that is, whether it is a pendulous breast or a small breast attached to the chest wall. In a general way, if the tumor is in a twelve or six o'clock position or in the upper or lower quadrant, the vertical incision can usually be best utilized to make a wide excision of the growth. I always make the widest excision possible of the tegmental structures surrounding the tumor. If the tumor is in the three or nine o'clock position a transverse incision will often permit a satisfactory and more adequate removal of the tegmental structures surrounding the tumor. It is difficult to state in centimeters the amount of surrounding skin to be excised as this depends on the type of lesion, whether it is an ulcerating or an infiltrating type of lesion, but when possible an area of 7 to 9 cm. from the growth should be excised. This is often difficult in lesions located in the extreme upper inner margin of the breast but an excision of this extent can be carried out in removing most of the axillary hair-bearing area and the wound can be closed without the use of skin graft by utilizing the latissimus dorsi muscle from the skin flap.

The majority of skin recurrences which we see occur in cases of ulcerating malignant lesions or the so-called inflammatory type of malignant lesion. In more than five per cent of our cases an ulcerating or inflammatory type of malignant lesion is present. Skin recurrence may occur even though a very wide excision of the skin has been made because the edema surrounding these lesions indicated malignant invasion of the skin and lymphatics. In cases of this type I have seen skin recurrence occur in distant areas such as the abdominal wall, back and scalp.

DR. GEORGE J. HEUER (New York): I do not intend fully to discuss Doctor Rodman's paper, but I cannot, without protest, accept his statement, that the Halsted operation results in such impairment of the function of the arm as to constitute a great disadvantage.

Doctor Rodman's statement that he has commonly seen function of the arm destroyed by a scar in the axilla following the Halsted operation is based, he admits, upon a few cases he saw at the Johns Hopkins Hospital in the very early days of this operation. Since that time the operation has been modified and improved, and I am quite convinced, from a very large experience, that the Halsted operation can be performed with a resulting axilla and with function of the arm quite as good as in any operation I have seen, including the Rodman operation.

The question raised by Doctor Rodman as to whether you shall skin graft or not skin graft perhaps deserves comment. One gets the impression from hearing men speak of skin grafting in connection with breast operations that skin grafting is a procedure which is either difficult or at least exceedingly objectionable. I do not think that such is the case.

One skin grafts in breast operations for a specific reason, and that is to secure closure of the wound without tension. It is a principle that is recognized, no matter where upon the body surgery is practiced.

If a surgeon chooses to remove so much skin—and I heartily agree with Doctor Rodman in everything he said about removal not only of a wide area of skin but also of subcutaneous tissue—that he can not subsequently close the wound without undue tension, then the only logical thing to do is to close it by means of skin grafting. I have had the opportunity in Baltimore, in Cincinnati, and in New York, of comparing, side by side, operations on the breast in which in one case skin grafting was used and in another case the skin was closed under tension, and I am convinced that a wound will be fully healed in a shorter time with grafting than with closure of the skin under tension.

DR. CHARLES C. LUND (Boston): There has been, as you know, a continuous interest in breast cancer in Boston, beginning perhaps in the nineties, or even earlier, with Warren, and then Greenough and Simmons of the Massachusetts General, and later Greenough, Simmons, Taylor, several others and myself, at the Huntington Memorial Hospital. Doctor Greenough was an advocate of the Rodman incision, and through his influence I was brought up to use it, and still use it, and like it. The work at both hospitals, has been published many times, and shows a long, continuous record of improvement. We feel strongly that any appreciable percentage of skin recurrence shows very inadequate planning of the operation or performing of the operation. I, personally, do not see why a Halsted operation would not give just as good results, if properly done, as described by Halsted, and reported on by Lewis and Rienhoff.

I do want to emphasize, though, the matter of choice of patients for radical breast operation. After roentgenograms of lungs, spine, pelvis and skull, exclusion from radical operation of any cases that have signs of metastasis there, and exclusion of cases with appreciable amounts of edema of the skin, or distant metastases of any kind. This all has been presented. The group working with Dr. Whipple have published identical findings. After operation, with wide skin removal, I rather feel the way Doctor Heuer does, that a skin graft is not a disgrace, even if you use the Rodman incision.

TABLE I

132 Cases—Radical Mastectomies—Rodman Method

61%—Free from all evidence of local regional or distant metastasis for	3 years
46%—Free from all evidence of local regional or distant metastasis for	5 years
16%—Free from all evidence of local regional or distant metastasis for	5-10 years
6%—Free from all evidence of local regional or distant metastasis for	over 15 years

TABLE II

132 Cases—Radical Mastectomies—Rodman Method

53%—Axillary metastasis at operation
23.5%—Free from recurrence for 5 years
46%—No axillary metastasis at operation
63.5%—Free from recurrence for 5 years
3—Local recurrences in entire group—2.2%

DR. WM. CRAWFORD WHITE (New York): Last year, before this Association, I read a paper on "Skin Removal in Radical Mastectomy." I refer you to that paper for details. But I desire to call your attention to the fact that primary cases, with no axillary metastases, had a local recurrence rate of 10.8 per cent, while primary cases with axillary nodes involved had a local recurrence rate of 31.5 per cent. This is in accord with several other large clinics, whether or not skin grafting had been practiced. These reports are based on both private and ward cases, grouped together. Doctor Rodman has given us a very low local recurrence rate in 150 private cases. Apparently considerable skin has been removed, although his measurements are not stated. I am at a loss to explain his low recurrence rate.

I am an advocate of the removal of at least a minimum diameter of 15 cm. of skin, but I am convinced that wider removal of skin will not reduce local recurrence. We must remember that Doctor Halsted practiced a wider excision of skin in his first 50 cases, yet he had a local recurrence rate of 31 per cent.

Local recurrence is due to cancer cells that have not been removed at the operation. We must remember that, in addition to the skin involvement in the neighborhood of the tumor, we have the other areas adjacent, in all directions; and, lastly, we must note the spread by lymphatic permeation and emboli to the intercostal and internal mammary

lymphatics. These latter areas are not removed in the most radical operation, and are the source of retrograde growth into the overlying skin in many cases. I think the last word on this has not been said.

DR. J. STEWART RODMAN (Philadelphia, Pa., closing): I repeat, in closing this discussion, that I only had time in fifteen minutes to touch upon a very few problems concerning cancer of the breast. All I was concerned with was the amount of skin removed, whether or not that bore any relationship or was important so far as local recurrences were concerned, whether local recurrences were unimportant or important, and whether the function of the arm had anything to do with the method of the procedure.

Many other problems, some of which were brought out by the gentlemen who have spoken, and I am very grateful to them for taking part in this discussion, I did not have time to touch on. I had to omit, toward the close of this brief paper, the matter of elephantiasis, or marked lymphadema of the arm. With the Rodman method this does occur now and again. I believe it occurs with any method that I know of, as far as that is concerned. I do not know exactly why. I think the combination of lymph blockage, with a mild infection of the axilla and arm resulting in scar tissue, may explain it, as suggested by Halsted.

We often have to "pie-crust," as Doctor Guthrie brought out, in closing these wounds. I think that pie-crusting is very useful in the procedure. It does seem to relieve a good deal of lymphatic block or of venous stasis at least, of the skin edges.

Occasionally we do get, even though it is always possible to close these wounds by extensive undermining of the skin, necrosis of the skin edges. This is never marked enough to require grafting to close the defect. I insist that this is not a plastic procedure. It is simply a closure of a wound made at a time when you do not know whether you are going to be able to close it or not, because you have removed enough skin in doing so.

As I see it, the objection to skin grafting is the resulting fixation of the scar to the chest wall; the fact that it is time-consuming; and, in our experience, is an unnecessary addition to the operative technic.

As to Doctor Horsley's discussion, there are many problems concerned that I did not go into, one of which is the matter of sterilization. We have tried that. We are still undecided as to whether it is of any value or not.

Of course, we all know of the tremendous amount of work that Doctor Harrington has done, and the beautiful results he has obtained. I, personally, have had no luck whatsoever with acute skin cancer. The cases he showed on the screen would be what I call cancer "en cuirasse." I do not know what he calls it, but to me that has been hopelessly fatal business.

I think the location of the growth, of course, is very important, as to where you plan your skin incision, but, nevertheless, we find with a skin incision such as we showed on the screen as the Rodman method, you can keep away from the edge of the growth, depending where it is, by varying the upper and lower line of the incision. We do not have to change the type of the incision depending on the location of the growth.

Now as to Doctor Heuer's remarks, I was very much pleased to hear him say what he did. I have never had the pleasure of seeing Doctor Heuer perform a breast amputation, and I am afraid I am a little old-fashioned in going back to my student days at Hopkins. I was not an undergraduate student there, but I was doing graduate work in pathology when Doctor Heuer was the resident in Surgery. Doctor Halsted, I recall very well at that time showed some 15 to 20 cases he had done by his method. Of course, that was the original procedure. No doubt it has been improved by Doctor Heuer, and others. But in the cases shown not one could get her arm above a right angle because of the bridge of scar tissue from the chest to the arm.

I have seen other cases since then, done by this method, and by good surgeons, that also could not get their arm above a right angle.

I do not believe that it is not possible to avoid this complication. All I said in my paper was that the cases I have seen done by Halsted's method resulted in a certain amount of impairment of the usefulness of the arm in abduction and extension, that unless marked edema occurs such limitation of motion never follows the Rodman technic.

PILONIDAL CYSTS AND SINUSES*

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THE HIGH INCIDENCE of pilonidal cyst or sinuses in members of the armed forces has resulted in this lesion becoming a major surgical problem in all military hospitals. In civil life, disability following treatment is usually not great, as the patient carries on his usual occupation during the greater portion of the healing period. A soldier, on the contrary, cannot undergo the extraordinary exertion of military duty with an unhealed wound. Healing often requires months, with the loss of many man-days.

In spite of much research, the etiology of these sinuses is not clear. Stone[33] notes a similarity to the preen gland of certain birds. Kallet[18] suggests an embryonic rest of a vestigial secondary sex gland. Tourneaux,[34] Herrmann,[34] Mallary,[25] and Gage[16] believe the cyst results from an abnormality in the development of the neural canal. Fréré[13] and Fox[15] stress an embryonic infolding of cutaneous epithelium. Kooistra[20] found evidence to support each of the latter two theories and states that no conclusive opinion seems justifiable.

There is also a great divergence of opinion regarding treatment. Among the ambulatory methods, the aim is to destroy the diseased tissue by physical or chemical agents. Anderson[1] injected chloride of mercury; Crookall,[9] silver nitrate; Biegeleisen,[2] fuming nitric acid. Cutler and Zollinger,[10] and, later, Block and Green[3] report successful results with a modified Carnoy's solution. Smith,[31] and, later, Turell[35] used roentgenotherapy on recurrent cases, with good results.

Kleckner,[19] in 1936, by means of a questionnaire from members of the American Proctologic Society, collected 4,699 cases. Of these, 4,231 had been operated upon by the open method, indicating that this was the method of choice among experienced proctologists. Cautery excision and open packing was first recommended by Stanton.[32] Rogers and Hall[28] and, more recently, Rogers and Dwight[27] have reported gratifying results with this method.

Following excision, closure of the wound has been advocated by many. Due to the difficulty of obliterating the dead space and of approximating the tissues, numerous methods have been described. Ferguson and Mecray[14] use a mattress suture of steel wire tied over a gauze roll on either side. Burgess[6] undermines the wound edges and uses silk retention sutures tied

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

over a sponge or gauze. Gage[17] stressed the value of sea sponge pressure to obliterate the dead space. Recently, Dunphy and Matson[12] described a method of undercutting the overlying tissue from the sacral fascia to facilitate closure.

Lahey,[21, 22] after block excision, filled the defect with a pedicle flap obtained from over the gluteus maximus. Later he modified this procedure by using a flap attached at both ends allowing the defect of the gluteal region to granulate. Cattell[7] used a similar procedure but closed the space over the muscle by converting it from a crescent into a Y.

Brezin,[4] in order to remove the scar from the midline, used a U-shaped incision circumcising the openings of the sinuses within the U. A pedicle flap was then reflected and the cyst and sinus tracts dissected out.

MacFee,[23] and De Prizio[11] recommend a partial closure, suturing the skin edges without tension to the sacrococcygeal fascia. This leaves a small raw area which heals by granulation. Colp,[8] in 1929, and, recently, Van Alstyne[36] described a similar method except that the skin edges were in approximation. Buie[5] does not remove the floor of the sinus overlying the fascia, and sutures the skin edges to the membranous edges of the sinus. This subsequently undergoes a squamous metaplasia.

Recently, good results have been reported by numerous military surgeons with various methods of treatment. Among these are: Pickett and Beatty,[26] using excision and packing; Woldenberg and Sharpe,[37] excision and primary suture; Scott,[30] using buffered sulfanilamide locally with primary suture; and De Prizio,[11] employing the skin to fascia type of operation.

A survey of these cases, in the Eighth Service Command, by Colonel Coley, the Surgical Consultant, revealed no uniformity of opinion as regards treatment, the great desirability of improving end-results, and the necessity of reducing morbidity. In studying the material of the Brooke General Hospital, as a part of the above survey, it was found that from January to October, 1942, there had been 77 cases treated by surgical excision. Fifty-six had healed and returned to duty, while 21 were still under treatment.

Of the 56 healed cases, half of them had electrosurgical excision, and the wound packed, while the remainder were excised and closed by primary suture.

In the 28 cases closed by suture, 12 healed primarily in an average time of 19 days. Sixteen cases became infected with subsequent opening of the wounds. From then on, these were treated by packing and healing occurred in an average of 69 days.

In the 28 cases treated by open packing, the average time of healing was 77 days (Fig. 1).

The study indicated a lower average healing time for the closed case subsequently breaking down than for the case treated by the open method. In addition, the average healing time of all closed cases was 47 days as compared with 77 days for the open method.

On October 16, 1942, the closed method was adopted for all cases. Excision was by scalpel. Meticulous attention was paid to hemostasis.

Cotton or wire suture replaced catgut. Great care was taken to avoid undue tension and to eliminate dead space. Pressure dressings, as advocated by Gage,[17] were employed.

FIG. 1

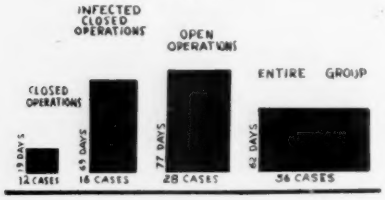


FIG. 2

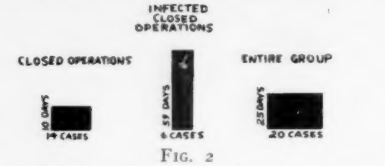


FIG. 1.—Average healing time of cases between Jan. 1 and Oct. 1, 1942.

FIG. 2.—Cases treated by excision and primary suture.

Twenty cases were treated according to this plan. Fourteen healed primarily in an average of 10.5 days. Six had postoperative infections, and healed by second intention in an average of 59 days. Cotton and steel wire were each used in 50 per cent of the cases. It seemed as if the wire wounds were superior (Fig. 2).

At this time, a new method of closure suggested itself to one of us (Frank C. Shute), which seemed to eliminate the difficulties of dead space and tension. A double elliptical incision is made in the skin surrounding the cyst and sinus tracts, and is carried down perpendicularly to the gluteal aponeurosis on either side. The block of tissue is dissected off the sacrococcygeal fascia and removed (Fig. 3). A lateral incision is now made through the gluteal fascia on either side, corresponding to the original skin incisions and is carried well into the muscle (Fig. 4). This creates an inner fibromuscular flap which is turned medially and sutured to its fellow of the opposite side. This fills in the area dorsal to the sacrum and coccyx eliminating the dead space (Fig. 5).

Cutting the fibers of the gluteus maximus mobilizes the lateral flaps so that it slides medially over the edge of the sacrum and can be sutured to the opposite lateral flap without tension (Fig. 6). The skin now falls together and is easily approximated (Fig. 7).

This method satisfactorily overcomes the difficulties of tension and dead space which are inherent in the other types of closure. In addition, the transplanted muscle furnishes an abundant blood supply to the base of the wound which is of great importance in healing.

Fifty-nine white males have been operated upon according to this technic. Most were in the third decade of life. The two outstanding symptoms were pain and discharge, while the objective signs were inflammatory induration, abscess or sinus formation. Not a single asymptomatic case was operated. Fourteen had abscesses which were immediately incised. The excision followed in an average of 8.6 days. Ten were recurrent cases and were prepared for an average of 5.6 days before operation. Thirty-five presented chronic infected sinus tracts and were prepared an average of 3.5 days. All cases were placed at rest and given hot sitz baths. No preoperative sulfa drugs were used. In some of our earlier cases the sinus tracts

FIG. 3

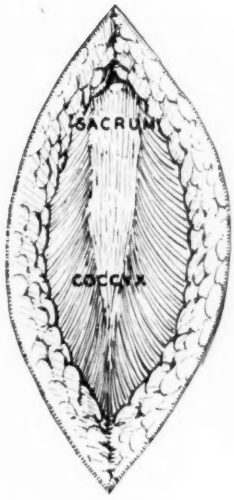
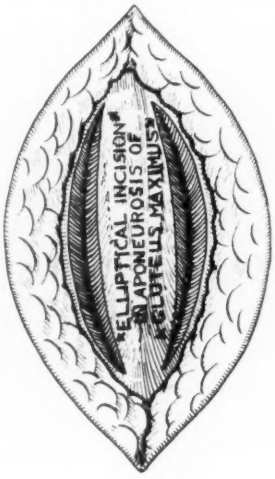
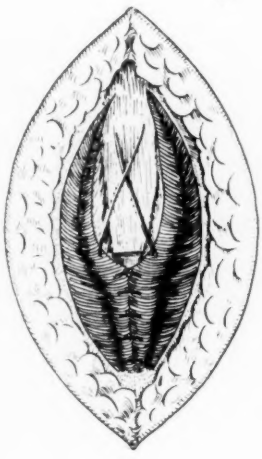
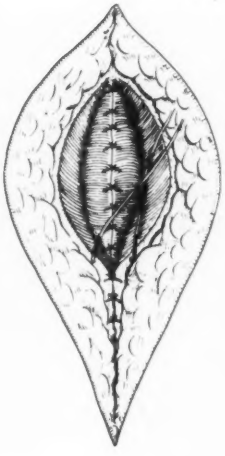


FIG. 4







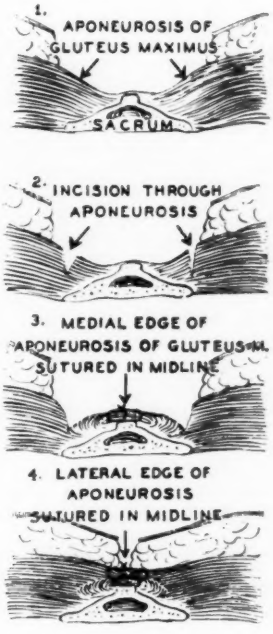


FIG. 5

FIG. 6

FIG. 7

FIG. 3.—The sinus has been excised exposing sacrococcygeal fascia and the aponeurosis of the gluteus maximus.

FIG. 4.—An incision has been made on either side through the aponeurosis of the gluteus maximus. It is not necessary to join the incisions at the ends of the ellipse.

FIG. 5.—The inner fibromuscular flaps are being sutured together in the midline.

FIG. 6.—Approximation of the outer muscular flaps.

FIG. 7.—The steps of operation in cross-section.

were injected with methylene blue; but we found, as did Rogers,[29] in which the dye filled the lymphatic trunks and gave a false impression as to the extent of the lesion.

The block of tissue removed usually measured about 12 x 8 cm. The largest block was 15 x 10 cm. In this case, the wound closed easily. Sinus tracts extending into the thigh were dissected out separately from the midline block in a few instances. The bacteriology of the lesions were carefully studied. The excised specimen was brought to the laboratory in a sterile towel. Its skin surface was saturated with alcohol, which was then ignited. An incision was made into the infected area and a loopful or two of material was streaked on eosin-methylene blue agar and tubes of lactose broth were inoculated for the determination of coliform organisms. Blood agar plates, tubes of thioglycolate broth and milk, and beef heart infusion broth were inoculated for other organisms. The routine blood plate procedure was found to yield 46 per cent negative findings, whereas, thioglycolate broth or skim milk yielded 95 per cent positive findings of streptococcus and staphylococcus infections. The latter media were very satisfactory for organisms which required more or less anaerobic conditions.

Thirty-nine specimens were examined and the following types of organisms were encountered:

(1) No organisms found	2
(2) Streptococci (hemolytic—3; nonhemolytic—8)	11
(3) Staphylococci (hemolytic—6; nonhemolytic—7)	13
(4) Mixture of staphylococci (predominantly hemolytic) and streptococci	8
(5) Anaerobic streptococci	5
(6) Coliform bacteria	None

In the specimens from recurrent cases, no epithelial tissue was found. Only sinus formation as a result of infection in a dead space was noted. This is in keeping with Roger's[29] findings; and we believe the majority of so-called recurrences are the result of incomplete obliteration of dead space.

Postoperatively, these patients were given paregoric for three days then mineral oil. Enemata were administered as indicated. Patients were allowed to be ambulatory as desired at the end of 12 to 24 hours. The sutures were removed on the fifth to seventh day. Pressure dressings were abandoned because they were unnecessary with this operation. They seemed to cause invagination of the suture line.

The results in these 59 cases are most gratifying. Forty-eight healed in an average time of approximately eight days. Eleven cases had postoperative complications. Three were accidents and eight infections. One patient fell out of bed, opened his wound on the fifth postoperative day. Another had a fecal impaction, and separated the lower one inch of his wound on the sixth postoperative day. The third, an unusually active man, opened an inch of his wound on the second postoperative day. These were pulled together with adhesive and healed in 15, 16 and 15 days, respectively.

Of the eight suffering infections, three were minor stitch abscesses and five were infections of the lower perianal angle of the wound. These infected cases healed in an average time of 22 days. The healing time for the entire group was approximately 11 days. When healed, the enlisted men returned to duty after an average convalescent period of three weeks, while officers returned in 10 to 20 days following operation (Fig. 8).

FIG. 8.—Cases closed by new technique.

The distributions with respect to time for healing are given in Table I, and curves showing the cumulative per cent of cases healing after various periods following operation, for the uncomplicated, infected and the combined series of cases, are shown graphically in Figure 9.

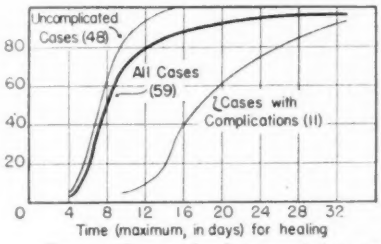


FIG. 9.—Curves showing cumulative per cent for periods of healing after excision of pilonidal cysts.

TABLE I

PERIODS FOR HEALING AFTER EXCISION OF PILONIDAL CYSTS

	Uncomplicated Cases		Infected Cases†		All Cases	
Time for Healing, in Days	No.	%	No.	%	No.	%
3 to 5	3	6.2	..	..	3	5.1
5 to 7	13	27.0	..	..	13	22.0
7 to 9	21	43.6	..	..	21	35.6
9 to 11	8	16.6	..	..	8	13.5
11 to 13	2	4.5	1	9.1	3	5.1
13 to 15	1	2.1	2	18.2	3	5.1
15 to 17	..	..	2	18.2	2	3.4
17 to 19	..	..	1	9.1	1	1.7
19 to 21	..	..	1	9.1	1	1.7
21 to 23	..	..	1	9.1	1	1.7
23 to 25	..	..	..	..	..	..
25 to 27	..	..	1	9.1	1	1.7
27 to 29	..	..	..	..	..	..
29 to 31	..	..	1	9.1	1	1.7
Over 31	.	..	1*	9.1	1*	1.7
Total	48	..	11	..	59	..
Average time	7.8		21.8		10.6	

† Includes three cases which sustained accidents.
* Fifty-three days.

In the series of 48 uncomplicated cases, it will be noted that 90 per cent were healed in less than 11 days, and all of them in 15 days or less. Even in the 11 cases in which stitch infections or other complications occurred, 70 per cent were healed in less than 23 days, and 90 per cent in less than 30 days. For the entire series (59 cases) it will be noted that 60 per cent were healed in as short a period as nine days, 80 per cent in 13 days, and 90 per

cent in 17 days. The period of healing extended beyond 25 days in less than five per cent of cases, the latter including one case which required 53 days and another 30 days.

No. 38-gauge stainless steel wire was used in the wound for ties, and No. 32-gauge wire for sutures. In our hands, wire has produced less reaction in tissue than catgut or cotton. It is not used on account of its supposedly great tensile strength. As a matter of fact, the finer grades break readily if undue tension is applied. In the skin around the perianal region a subcuticular suture of wire is very satisfactory. In the remainder of the wound interrupted sutures were used.

Buffered sulfanilamide was used in the first 29 cases. It seemed to cause an excessive amount of oozing and serum in the wounds. Nine of the 11 complications occurred in these cases. In the latter 30 cases, in which sulfanilamide was not used, there occurred only two complications.

An accurate evaluation of end-results must, of course, await a more extensive employment of the method and the passage of further time. However, the many advantages of the operation, and its ready adaptability to war conditions, has led to its presentation at this time. None of the 59 cases have, so far, returned with a recurrence.

SUMMARY

The experience with pilonidal cysts and sinuses at the Brooke General Hospital is reviewed.

An operation is described which is found to be far superior to any previously used by the authors. A wide, double elliptical incision is carried perpendicularly downward to the fascia of the gluteus maximus. The circumscribed tissue block is separated from the sacrococcygeal fascia and removed. A lateral incision through the gluteal fascia in the line of the original incision is now made on either side. It is deepened into the fibers of the gluteus maximus and the fibromuscular flap thus created is turned medially and sutured to its fellow of the opposite side, in the midline.

This fills in the area dorsal to the sacrum, eliminates the dead space, and furnishes an abundant blood supply to the base of the wound. The lateral flap slides medially over the edge of the sacrum and is sutured to the opposite lateral flap without tension. The skin is now easily approximated.

Results of this technic in 59 cases are presented. Forty-eight healed primarily in an average time of eight days. Eleven cases had postoperative complications, and healed in an average time of 22 days. The healing time of the entire group was 11 days.

Bacteriologic examination of 39 excised cysts disclosed viable organisms in 95 per cent of the specimens. Nonhemolytic streptococci and hemolytic staphylococci constituted the predominating flora; in five instances only anaerobic streptococci were found, and it is interesting to note that coliform bacteria were absent.

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DISCUSSION.—DR. HARVEY B. STONE (Baltimore): Ever since Doctor Finney demonstrated a case of pilonidal sinus to my third-year class at the Medical School, I have been interested personally in this curious and provocative lesion. It certainly has been, in the last few years, provocative of a remarkable outpouring of publications, but that has not always been true. It was only about 16 or 18 years ago that I read a paper on this subject before the Southern Surgical Association, reporting a group of some 60 cases, and after the meeting was over, several widely experienced surgeons told me that they had known little or nothing about pilonidal sinus before and did not believe they had ever recognized a case, and several, not quite so frankly, said they did not believe that I had seen as many as I had reported.

I do not believe that the latter doubt will exist in anybody's mind now, after the numerous publications have come in and after the experience of Induction Boards and army surgeons with the really wide prevalence of this lesion.

There are a number of interesting problems—its embryologic origin; the reason for the defect in embryology which produces it; and the difficulty from the practical, clinical side in securing rapid, firm, and enduring healing after removal.

It is with the latter problem that Colonel Burch's paper deals, and I think there are at least three recognizable causes of trouble in securing desirable results: One is infection, and his emphasis on the spending of some time preparatory to operation in cleaning up an infection I think is a point of very great practical importance. A second is the complete and adequate removal of the lesion itself. A third is the dealing with the resultant wound.

So great has been the difficulty in dealing with the wound that a number of writers on the subject have frankly abandoned any attempt to close it and advocate that it be dressed open and left open to heal by granulation. Others have gone further, and have even abandoned attempts at excision and treat the lesion by some method of chemical or electrical destruction, in order to avoid an open wound altogether, and a great many have published papers describing various methods of plastic closure or suture, designed to obliterate the dead space.

This paper of Doctor Burch's I think falls clearly in this last group. Personally, I believe that closure should be undertaken, and that it is an unnecessary surrender to pack it open and wait for it to granulate. The reason that I feel so is because, as the statistics of Doctor Burch have shown and those of others who have advocated somewhat different plastic closures have indicated, where closure is attempted a considerable percentage of primary successes are obtained. That is "all to the good," and even where closure fails, and where the wound then has to be treated as an open wound and allowed to fill up by granulation, the period of deferred healing is probably less than if no attempt at closure had been made in the first instance.

So I believe we should accept the principle of an effort at closure, and that that effort entails some plan to obliterate the dead space. The dead space has a noncollapsible, bony floor. It has edges which are difficult to approximate without tension. Therefore, the introduction of any principle which will overcome these difficulties, which will help to close the dead space and bring together the wound edges in proper position for healing, so that they are neither inverted into the depth of the wound nor under great tension in being approximated, is highly desirable and is, I think, the sound principle to proceed on.

I think that Doctor Burch's method is ingenious, and that it is based on fundamentally sound conceptions. He certainly has presented a laudable record of success so far, and we all hope that he, and others, will give this method wider employment and report further as to its success.

DR. FRANK H. LAHEY (Boston): I wish to speak, just briefly, about this subject because, being responsible for a little of the literature, I feel interested. I feel particularly interested, however, because of recent inspections of Naval hospitals, and in the course of the inspections seeing pilonidal sinuses in Army hospitals and seeing the number of duty-days saved by primary suture.

I came yesterday from the United States Naval Hospital in Norman, Oklahoma. There, in the Surgical Service they have now excised 15 consecutive pilonidal sinuses, with average hospitalization of 19⅝ days.

I recently saw the Torney General Hospital in Palm Springs, California, an Army hospital, where Doctor Beaver had had 14 consecutive pilonidal sinuses treated by excision, closure averaging, again, under 3 weeks.

In my mind, the problem is quite different for the men in the service and for those in civilian life. In the service the important thing is man-hours, but equally important is beds. When one realizes that Doctor Beaver reports his series as averaging 19 days' disability, and the Naval Hospital at Norman, 15 days, that the Navy and the Army are seeking additional beds, and that these patients, unlike those in civilian hospitals, occupy beds until surveyed to duty, this is, I believe, in the Army and Navy quite a different problem from that in civilian life.

Just now I spoke to Doctor Cattell because he has been interested in pilonidal sinuses in civilian practice. The plan of Horatio Rogers in Boston, who advised the plan of local excision, is applicable in an office or in an out-patient department. If these people are so situated that they can get away from their work or their school long enough to obtain this daily or alternate-day treatment, then I feel that the method of local excision with granulating in, is permissible. The Army has a different problem, however, and has demonstrated, I think, in many of the military hospitals that excision will work; does save hours; and certainly does save beds.

DR. HENRY F. GRAHAM (Brooklyn): I was recently stopped by a man who wanted to inquire about his son. He said his son was in the Army and he had had three operations upon the base of his spine, but he knew they must have been good operations because they were all done by Majors. I am sure it was not performed by Colonel Burch.

There is one little step that I have employed, that I think, in some cases, perhaps only in civil life, is of value in diminishing the infection at the time of excision. It is something that can be done in addition to these steps that have been recommended by Colonel Burch, and which seemed so sound and good to me. I am going to try his method.

I often use an electric cutting current and make a vertical incision through the infected cyst or sinus, laying it wide open. It is then wiped out, the edges are held apart, and, with a bipolar current and a heavy, round-tipped needle, I fulgurate the base of the wound until the entire lining of the cavity has been destroyed to a depth of about one-eighth of an inch. Then, when it is entirely dry and the infection theoretically has been mostly eliminated, the excision is made.

I see no reason why that could not be done first, and the method of Doctor Burch used after that, if you do not carry bipolar fulguration so deep as to destroy the underlying tissues. This will destroy a great deal of infection, and our results have been much better since we have used this method than when we undertook simple excision.

DR. JAMES M. MASON (Birmingham, Ala.): The renaissance of pilonidal sinuses and cysts has been extremely interesting. After years of only casual comment, the subject has been given a prominent place in surgical literature by the large number of cases that have been reported during the past six months.

My attention was first directed to this anomaly by a paper that Harvey Stone presented at the meeting of the Southern Surgical Association in 1923. He stated that "less than a dozen original articles had been found in a fairly extensive search covering the previous sixty years." The literature since the appearance of Stone's publication has been singularly barren of contributions until within very recent months. Beginning about November, 1942, reports, from Army hospitals particularly, are appearing in

increasing numbers. These reports discuss the management of the large numbers of pilonidal sinuses that are applying for treatment in Army hospitals in all sections of the country.

A review of the discussions of the embryology of the sinus is interesting. As far back as 1892, Mallory came to the conclusion that the sinus resulted from failure of obliteration of the caudal canal. This view had been previously expressed by Hermann and Teureux, and other European investigators. Stone has not accepted this view, and holds to the theory that the sinus results from a "special local downgrowth of epithelium originating from the true skin and not from the medullary groove."

In 1935, two noteworthy publications appeared; one by I. M. Gage, Archives of Surgery, August, 1935, entitled "Pilonidal Sinus: An Explanation of its Embryological Development"; another by S. L. Fox, Surgery, Gynecology & Obstetrics, February, 1935, entitled "The Origin of Pilonidal Sinus; With an Analysis of its Comparative Anatomy and Histogenesis." Gage supports the theory of failure of obliteration of the medullary canal. Fox upholds the theory of downgrowth of epithelium. Ewing, discussing tumors and anomalies in the sacrococcygeal region says that "the entire group is not only numerous but complicated, and a rigid classification is at present impossible" (Neoplastic Diseases, Fourth edition, page 1006).

Regardless of views concerning embryology, surgeons recognize that cure should be sought by excision and closure of the wound.

Another matter of surprise is that with large numbers of young men in college taking part in football, baseball, and every sort of athletic activity, the cyst has attracted but little attention; nor, so far as I recall, did it give rise to any material trouble among the troops in World War I. Of course, the same relative numbers of pilonidal sinuses among a given number of individuals should not differ from time to time. Army surgeons claim that the extreme activity carried on in the training period is responsible for the infections and abscesses that bring the soldier to the hospital for medical attention.

Stone and Gage have advocated excision and closure, after proper preparation. They have, likewise, directed attention to the difficulty of completely obliterating the dead space at the bottom of the wound and of the value of compression in assisting in this obliteration. Looking at the illustrations of Colonel Burch's ingenious operation, it seems to me that there must still be a dead space undeneath the flaps of gluteus muscle, and that a pressure dressing should still be employed to obliterate.

COLONEL JOHN C. BURCH, M.C. (closing): The success of this operation depends upon filling up the dead space by means of flaps derived from the gluteus maximus muscle. Mobilizing the medial flaps, likewise, mobilizes the lateral flap and allows them to slide in readily.

The wound must be absolutely dry. Nonabsorbable sutures are preferred. Thirty-eight-gauge stainless steel wire for ties and No. 32-gauge for sutures has proved very satisfactory.

One cannot be too careful about infection; it can nullify any operative technic. Most of our complications come from operating too soon. The best preventive for infection is an adequate preparation of the patient.

Our experience with sulfanilamide has been quite interesting. In the first 29 cases, we used a buffered sulfanilamide. It seemed to cause oozing and the accumulation of serum in the wounds. Nine of the 11 complications were in this group.

EFFECTS OF ETHER AND CYCLOPROPANE ANESTHESIA UPON THE RENAL FUNCTION IN MAN*

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SEVERE ACUTE ACID-BASE EQUILIBRIUM DISTURBANCES and changes in the regulation of body water exchange are seen too frequently during the postoperative period. They occur in spite of seemingly well directed fluid therapy. Although it is generally recognized that alterations in renal function are responsible for many of these changes, the etiologic factors and the specific changes in kidney function that are involved must be known before therapeutic measures can be employed objectively to correct them and to prevent them.

In an attempt to determine whether the anesthetic agent that was employed had any direct effects upon the kidney, renal blood flow and filtration rates were studied simultaneously in human beings preoperatively, during or immediately following operation (patient anesthetized), and in some instances postoperatively.

METHODS.—Seven patients who were to be operated upon under ether anesthesia and four who were to be operated upon under cyclopropane anesthesia were selected for study. The operative procedures were varied (Tables I and II). No attempts were made to alter the routine preoperative or operative procedures. To establish a normal for each individual, preoperative inulin and diodrast studies were run before each operation. About an hour before the operation, a hypodermic injection of morphine and scopolamine was given. A solution of 5 per cent glucose was administered during the operations. Inulin and diodrast studies were started near the end of the operation and were carried through the recovery stage.

The inulin and diodrast clearances were carried out, respectively, according to the technic of Alving, *et al.*,[2] and Smith, *et al.*,[4] as modified by Foā and Foā.[3] Two Gm. of inulin and 5 cc. of a 35 per cent solution of diodrast were injected intravenously. Fifteen minutes were allowed for this to mix thoroughly in the blood. The bladder was then emptied of urine and the clearance period was started. Two blood samples were obtained at ten-minute intervals. The clearance period lasted for 30 minutes and, at that time, the bladder was again emptied and washed. From the blood and urine concentrations, the clearances were computed. In those cases where changes

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were encountered, attempts were made to obtain postoperative studies. These were carried out one week after the operation. All the cases were adequately hydrated and were in acid-base equilibrium, as far as could be simply determined. All anemias had been corrected and no significant cardiac disease was present. All individual temperatures, during the studies, were within normal limits.

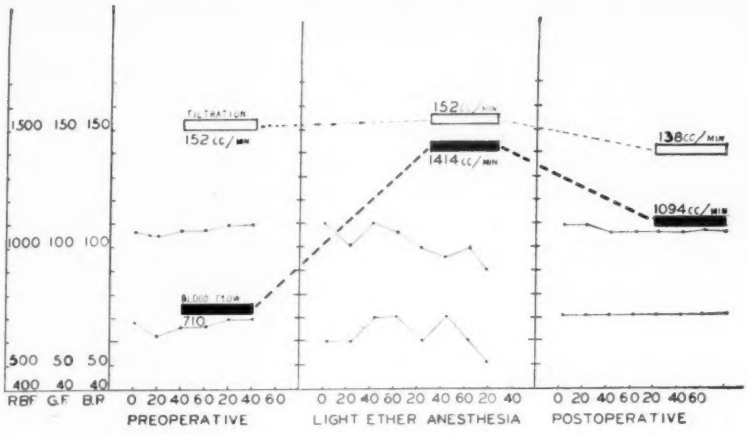
RESULTS.—Figures 1, 2, and 3 illustrate the variations in renal blood flow and filtration rates under ether anesthesia (Consult Table I for data that is not included in these figures).

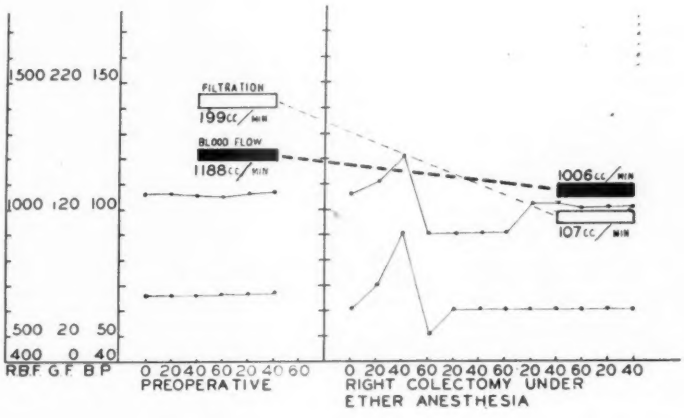
TABLE I

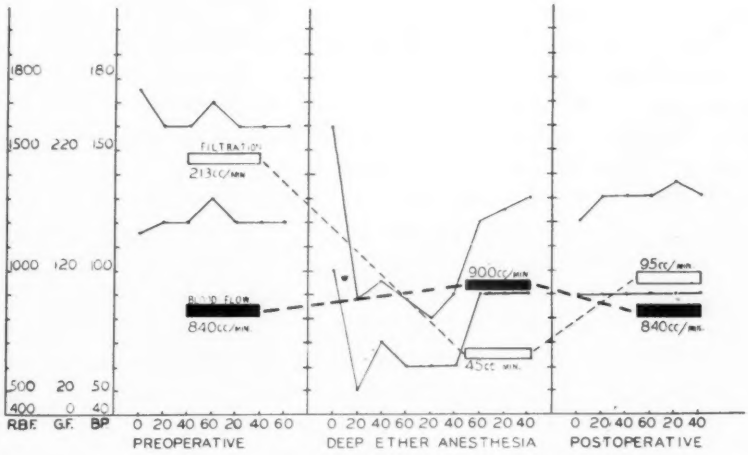
Case	Sex	Age	Type of Operation and Duration	Anesthetic Agent	Preoperative, Operative or Postoperative	Average Blood Pressure	Effective Renal Blood Flow, Cc./Min.	Filtration Rate, Cc. Plasma/Min.	Filtration Fraction C_i/C_p%	Tubular Excretory Mass mg. 1 Per Min.	Total Filtration 30 Min.	Urine Excreted 30 Min.	Per Cent Reabsorbed
No. 1 A.M.	F	33	Combined A.P. resect. of rectum	Ether	Preop.	105/65	1187.8	198.6	22.8	54.6	4958	570	80.5
					Operat.	100/60	1006.4	107.8	18.7		3234		
No. 2 M.H.	M	37	Combined A.P. resect. of rectum	Ether	Preop.	125/80	1449.1	138.3	19.2	64.3	4149	355	91.4
					Operat.	120/70	1369.0	140.7	19.8		4221	36	99.2
No. 3 E.B.	F	45	Hernia	Ether	Preop.	105/70	710.0	152.6	34.7	24.	4578	294	90.3
					Op.	90/50	1414.7	152.7	17.4		4581	76	98.3
					Postop.	110/70	1094.0	138.4	20.2		4152	250	94.0
No. 4 J.M.	M	33	Plastic, 3 hrs.	Ether	Preop.	120/90	680.9	80.6	21.1	34.6	2418	385	84.1
					Op.	125/90	852.0	110.0	21.5		3300	38	98.8
					Postop.	120/70	839.5	101:7	19.9	36.5	3051	420	86.2
No. 5 J.H.	M	62	Hernia, 2 hrs.	Ether	Preop.	170/120	785.0	224.3	53.1	33.7	6729	46.5	99.3
					Preop.	165/100	844.0	213.0	47.8	31.5	6390	300	95.3
					Op.	90/60	900.0	45.1	9.3	38.0	1353	85	93.7
					Postop.	170/105	841.5	95.0	20.6		2850	424	85.1
No. 6 R.S.	F	58	Resection rt. colon, 4 hrs.	Ether	Preop.	160/90	1045.7	140.3	20.0	30.6	4209	416	90.1
					Op.	120/70	817.0	47.2	8.5		1416	20	98.6
					Postop.	170/100	810.0	232.0	36.4		6960	402	94.2
No. 7	M	54	Suprahyoid, 3 hrs.	Ether	Preop.	120/80	740.1	73.7	19.6	31.3	2211	236	83.9
					Op.	120/80	1230.6	122.0	19.8		3660	56	98.5
No. 8	M	36	Total gastrectomy	Avertin-ether	Preop.	110/75	725.5	126.3	32.8	27.8	3789	338	91.1
						90/50	18.4	1.1	10.7		33	17	48.5

Four patients of variable ages, weights, and sex, who were anesthetized for periods of time varying between one and four hours, suffered no significant changes in either renal blood flow (diodrast clearance), or filtration rate (inulin clearance) as a result of anesthesia and operation. The low preoperative blood flows in two cases (Cases 3 and 7, Table I) are considered to be due to nervous factors during the first determinations. This concept is supported by the subsequent observation that the postoperative flow was normal (Case 3, Table I). Therefore, the increases in renal blood flow (Cases 3 and 7) between the preoperative and the operative determinations are not considered to be experimentally significant. Two patients (Cases 1 and 5, Table I) suffered diminution in the rate of glomerular filtration without a fall in renal blood flow. One (Case 5) experienced a sustained decrease for one week following his operation.

During, or immediately following, thoracoplasties performed under cyclo-







FIGS. 1, 2 and 3.—The effects of ether anesthesia upon inulin and diodrast clearances in man.

propane anesthesia, glomerular filtration rates decreased significantly in all of the patients studied (Figs. 4, 5, 6 and 7, and Table II). Renal blood flows were variable, two increased (Figs. 4 and 5) and two decreased (Figs. 6 and 7). One of the increased flows was observed while blood and pulse pressures were lowered (Fig. 5). The two patients in whom decreased renal blood flows were noted had low blood and pulse pressures during the tests (Figs. 6 and 7). In one instance (Fig. 7) "total" renal failure occurred. The urinary outputs, in spite of large amounts of intravenous and oral fluids, were low during the first 24 hours postoperatively (Figs. 5 and 7).

TABLE II

CYCLOPROPANE SERIES

Case	Sex	Age	Type of Operation and Duration	Preoperative Operative Postoperative	Urine Volume in Cc.	Sodium M.E.Q. Liter	Chloride M.E.Q./Liter	Ammonia M.E.Q. Liter	Total Nitrogen Gm. Liter	Inulin Mg./Liter	Inulin Clearance Glomerular Filtration Rate Cc./Min.	Diodrast Iodine Clearance Cc./Min.	Effective Renal Blood Flow Cc./Min.	Total Filtrations 30 Minutes	Urine Output 30 Minutes	Per Cent Reabsorption
No. 1 F.W.	M	40	Lateral thoracoplasty, $1\frac{3}{4}$ hrs.	Preop.	136	....	20.7	....	.....	2,298	144.6	485.0	831.0	4,338	136	96.8
				Operat.	35	74.5	85.4	....	.....	11,180	78.7	502.0	929.0	2,361	35	98.6
No. 2 B.M.	M	22	Second stage T.P.L., $2\frac{1}{4}$ hrs.	Preop.	610	12.1	14.9	6.4	0.997	1,309	120.6	750.0	1,225	3,618	610	83.1
				Operat.	16	22.6	7.2	33.5	3.157	24,593	83.1	614.0	1,100	2,493	16	98.9
No. 3* P.S.	M	45	Second stage T.P.L., $2\frac{1}{2}$ hrs.	Postop.	46	63.9	45.5	39.2	11.315	17,552	153.3	758.0	1,239	4,599	46	99.0
				Operat.	25	3.6	11.7	10.5	1.080	14,572	75.6	1,123.0	1,824	2,268	25	98.8
No. 4* P.B.	M	23	First stage thoracoplasty, 3 hrs.	Postop.	330	10.9	15.0	3.8	1.231	2,664	125.1	636.0	1,051	3,753	330	91.2
				Operat.	44	73.0	113.2	33.8	9.414	1,833	4.5	50.8	98	135	44	67.4

* Prodromal shock cases, 3 and 4.

The one patient who had an ether-avertin anesthesia (Case 8, Table I) showed a severe decrease in both renal blood flow and filtration rates. Further observations on the effects of avertin-ether and avertin anesthesias are now in progress.

DISCUSSION.—The inulin (glomerular filtration) and diodrast (renal blood flow) clearances of a comparatively large number of patients who are operated upon under skilled ether anesthesia do not decrease (Table I, Cases 2, 3, 4, and 7). In two instances (Cases 1 and 5, Table I), the filtration rate decreased with anesthesia but renal blood flow was not changed significantly. The lower filtration rate during anesthesia in Case 1 (Table I) was still within normal limits. However, in Case 5 the filtration rate declined 78 per cent, and was far below normal immediately following the operation. One patient (Case 6) suffered significant falls in both the rate of filtration and renal blood flow during the operation.

In view of the relatively large number of patients who showed no significant changes in inulin or diodrast clearances during light or moderately deep anesthesia, even though the anesthesia was prolonged, it is felt that any changes that occurred in glomerular filtration rate and in renal blood flow (tubular excretion of diodrast) during operation under ether anesthesia, were probably the result of factors other than the possible primary action of the anesthetic agent upon the kidney parenchyma. It is probable that in one instance (Case 5, Table I) a severe vasomotor control derangement due to an overdose of ether was the direct cause of the relatively

severe and prolonged reduction of the filtration rate. The operation was simple, a bilateral inguinal herniorrhaphy, and blood loss was minimal. The low operative filtration rate existed concomitantly with low blood and pulse pressures. The fall in pulse and blood pressures occurred while an inexperienced anesthetist was carrying the patient in plane 4, S III.* What part his mild hypertension may have played in the picture is unknown. His urine did not contain blood, casts, or albumin. The significant decreases in both renal blood flow and glomerular filtration rate in Case 6 (R. S.)

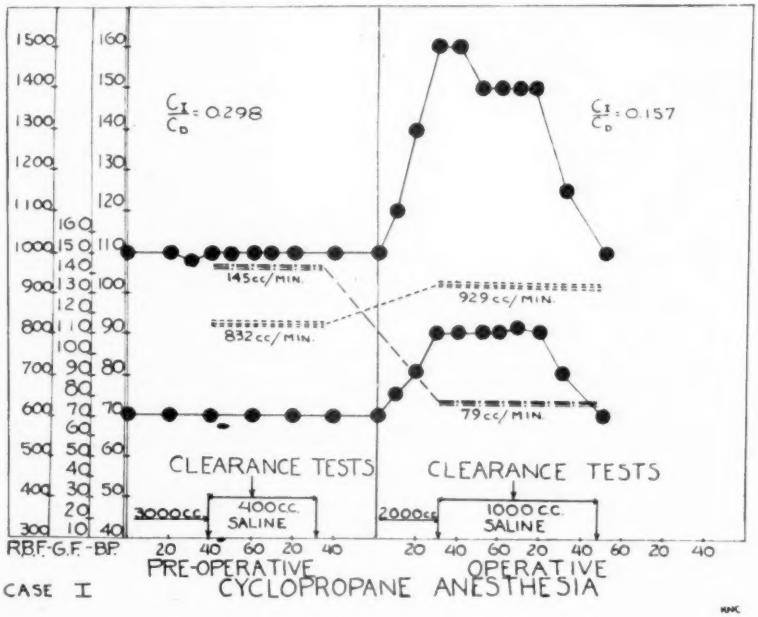


FIG. 4

were possibly due to an acute blood volume reduction incident to an extensive and prolonged operation.

The observation that the glomerular filtration rate fell in all of the patients studied during cyclopropane anesthesia, regardless of renal blood flow or blood pressure changes, seems to indicate that a direct effect of the anesthetic agent upon vasomotor mechanisms may be responsible for these changes. However, in this series of experiments no data pertinent to acid-base equilibrium are available. Without such data one cannot rule out the possibility that the respiratory acidosis, which is usually associated with cyclopropane anesthesia, may have been directly responsible for the diminution in the glomerular filtration rates, especially in those cases in which renal blood flow increased.

There is no evidence in either group of observations that anesthesia, blood volume flow reduction, or other variations from the normal incident

* Plane 4, S III denotes surgical anesthesia with complete intercostal paralysis.

to surgery effect any changes in the reabsorptive capacities of the renal tubules. The fraction of the glomerular filtrate reabsorbed by the tubules was either the same or greater during anesthesia than the controls in all patients except two (Case 8, Table I and Case 4, Table II). The respective urinary ionic and nitrogen concentrations in the preoperative and operative urines of Case 8, who suffered a decrease in the reabsorption fraction of glomerular filtrate, are not known, so that no statement can be made regarding tubular function. However, in Case 4 (Table II) the concentrations of the sodium ion, the chloride ion, ammonia nitrogen, and total urinary nitrogen

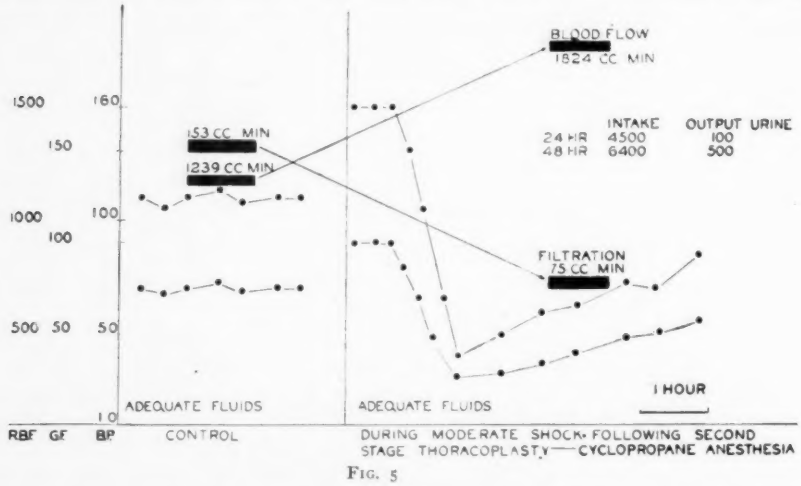


FIG. 5

were 6.6, 7, 8, and 7.8 times greater during the period of low fractional reabsorption (anesthetic period) than they were during the postoperative period of high reabsorption. The urine flow during the latter period was seven times greater than it was during the former. Therefore, although granting that these relationships may be fortuitous, since no attempt at balance control was made, it is probable that no great decrease in tubular reabsorptive capacity occurred during anesthesia in this instance, although the fraction of glomerular filtrate reabsorbed decreased, because the ionic and nitrogen concentrations and urinary flows underwent equivalent reciprocal changes. The relatively high concentration of ammonia nitrogen in the urine collected during anesthesia from Case 4 (Table II) indicates that the tubular cells retained their capability of effecting deamination of amino-acids and, therefore, were still capable of a considerable base saving—a tubular function of importance—in spite of anesthesia and a very low renal blood flow. Also, it is of interest that glomerular capillary permeability was not grossly increased by anesthesia or reductions in renal blood flow because no albumin or red blood cells were found in the operative or postoperative urines.

The lack of evidence for a gross increase in glomerular capillary permeability, for decreases in tubular excretion and reabsorptive capacities, or for

an increase in tubular permeability during ether and cyclopropane anesthesia, indicates that the variations in glomerular filtration rates and urinary outputs during and following the administration of these anesthetic agents are probably due, in the greater part, to primary derangements in acid-base equilibrium, in body water and ion distribution, and in cardiovascular functions incident to anesthesia, blood loss, and visceral trauma. Therefore, direct solutions of the problems concerned with the maintenance of homeostasis, especially in regard to acid-base equilibrium and renal function, during

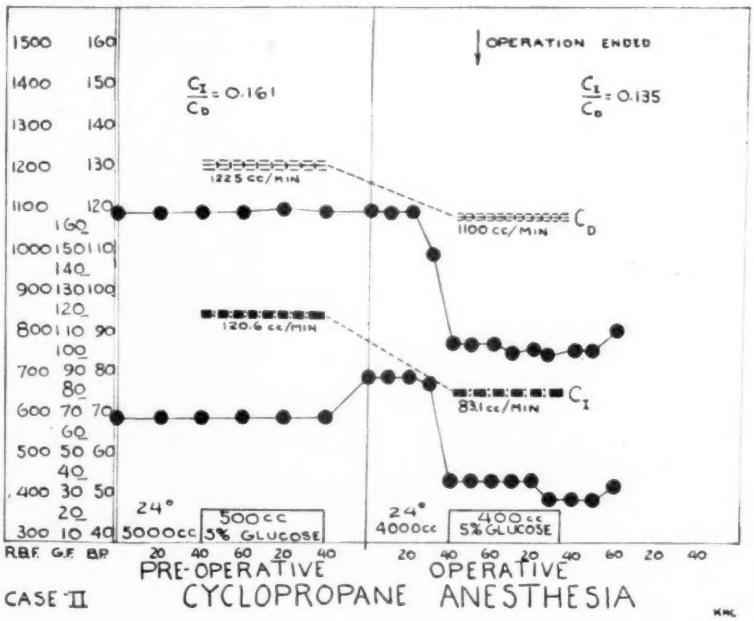


FIG. 6

and immediately following operations performed under ether and cyclopropane must await further studies of water and ion distribution, and acid-base balance in man under conditions that pertain to anesthesia and surgery. Although the solutions to these problems will necessitate the expenditure of a great deal of effort and time, it is likely that they will be more practical of solution than they might have been should ether and cyclopropane have a direct effect upon the kidney parenchyma.

CONCLUSIONS

1. Inulin and diodrast clearances are not affected by ether anesthesia provided that the anesthesia is well controlled and significant blood volume reduction does not occur.

2. The inulin clearances of all the patients studied were depressed during cyclopropane anesthesia; the simultaneous diodrast clearance changes were variable; two increased and two decreased during anesthesia.

3. Evidence was obtained that ether and cyclopropane had no gross effect upon glomerular capillary permeability, tubular reabsorptive capacity, tubular permeability, or tubular deaminization of amino-acids (ammonia production).

4. Because of the failure to demonstrate any deleterious action of ether or of cyclopropane upon the kidney parenchyma, the variations in glomerular filtration rate and renal blood flow, that occur during anesthesia, are probably, in great part, due to a combination of the "extrarenal" actions of these agents and the operative procedures. The disturbances in acid-base

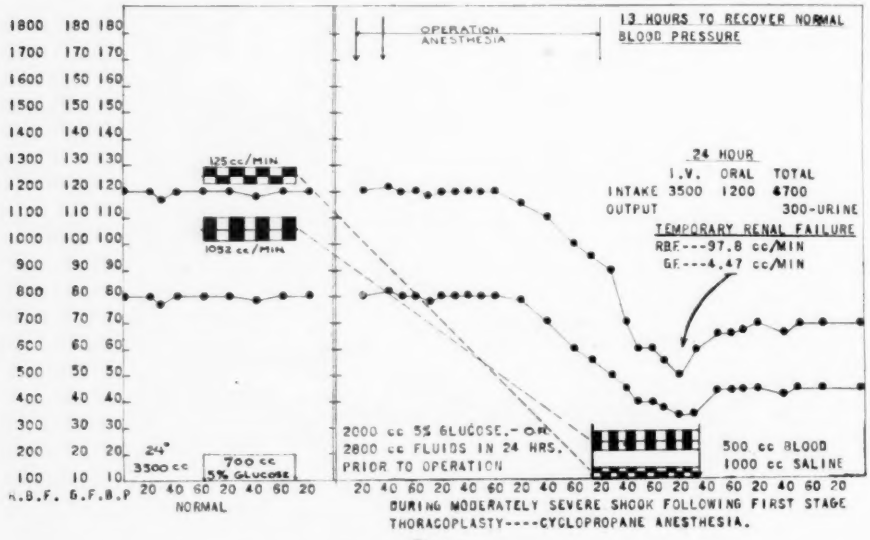


FIG. 7

FIGS. 4, 5, 6 and 7.—The effects of cyclopropane anesthesia upon inulin and diodrast clearances in man.

equilibrium, body water and ionic distribution, ionic concentration, and cardiovascular function, that are associated with disease, anesthesia, and surgery, are considered to be the primary causes for postoperative oliguria. (See the appended summary of earlier experimental work regarding the effects of anesthesia upon kidney function).*

*SUMMARY OF EARLIER EXPERIMENTAL WORK

Pringle, *et al.* (1905) Ether. Oliguria, depression of sodium and nitrogen excretion. Brit. M. J., **2**, 542.

Hawk (1911) Ether. Oliguria, elevation of NPN for 5–14 days in some cases. J. Biol. Chem., **4**, 321.

Miller and Cabot (1915) Ether. PSP excretion in 335 patients—average depression —20%, with fairly rapid recovery. Arch. Int. Med., **15**, 369.

Mac Nider (1920) Ether. 131 dogs—43 became either temporarily or permanently anuric. Related to age, fatty infiltration in kidneys. No response to diurectics unless "glucose protection" had been afforded. J. Pharmacol. and Exper. Therap., **15**, 249.

Luckhardt and Lewis (1923) Ethylene. Safe from standpoint of not producing anuria. J. A. M. A., **81**, 1851.

Marx (1931) Chloroform, Ether, Chloral Hyd. Edema more easily produced in animals by infused salt solution if anesthetic is given. J. Pharmacol. and Exper. Therap., **41**, 483.

Walton (1933) Amytal, Avertin, Ether. Recovery of diuresis slowest after barbiturates. J. Pharmacol. and Exper. Therap., **47**, 141.

5. The observations reported concerning the effects of ether upon kidney function are in agreement with the earlier observations of Smith[5] concerning the effects of spinal anesthesia upon renal function.

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DISCUSSION: DR. FREDERICK A. COLLER (Ann Arbor, Mich., closing): As Doctor Moyer stated, there are many things that we do not know about this whole problem, and we do hope this is a start on the final elucidation.

There is no question but that, usually, in the healthy person these alterations in kidney function are unimportant and the patient goes merrily on to recovery. Occasionally, however, the depression of kidney function that may be associated with prolonged anesthesia, prolonged operation, and perhaps the associated loss of blood may well be important, and even be the cause of death.

In the presence of certain states, that we can briefly summarize as malnutrition, where there is hypoproteinemia, or profound or even moderate anemia—these abnormalities in kidney function may be accentuated. I wish to present two cases in which the administration of the wrong kind of parenteral fluid nearly led to the death of the patients.

Case 1.—G. B., age 36, had had a subtotal hysterectomy. The operation was performed under nitrous oxide-ether anesthesia; the anesthesia was carried for four hours. During the day of operation and for the first four postoperative days one liter of saline solution was given intravenously in addition to 2500 cc. of other fluids (water by mouth and 5% glucose by vein). On the fifth postoperative day she began to vomit, and gastric drainage was instituted. 2500 cc. of saline solution were given daily in addition to 2500 cc. of 5% glucose solution for the next five days. During this later period her distention increased rapidly, urine flow decreased, respiratory difficulties appeared, and peripheral edema was noted. On the tenth postoperative day her condition approached *extremis*, and it was decided to pass a Miller-Abbott tube into the duodenum through a gastrostomy. Upon opening the abdomen four liters of ascitic fluid was obtained, and her distention was relieved. This fluid contained 2.79 Gm.% of protein (a/g ratio of 1.71).

For the next four days her urinary output exceeded her oral water intake, and her edema disappeared. She recovered.

The amount of salt that was given to her would be readily handled by a healthy individual but she could not do so. Why? We believe that the following physical abnormalities were collectively responsible: 1. Anemia (Hb. —54% S.); 2. hypoproteinemia; and 3. operative obstruction of the right ureter.

The parentral administration of salt solution in the face of these variations from normal resulted in a general deposition of fluids in tissues and body cavities. The deposition of fluid in the body cavities was associated with a large loss of serum proteins; in fact, she had as much serum protein in her abdominal cavity as she had in her blood stream (4,000 x 2.79 = 111.0 Gm. in the ascitic fluid) and 1,750 (calc. plasma vol.) x 5.4 = 94.5 Gm. in the blood vessels). This finding is particularly interesting in that it is fundamentally similar to Blalock's observations concerning the effects of parenteral saline given to animals in shock.

To summarize, this case illustrates the protein "washing out" effect of relatively small amounts of saline solutions when given in the face of anemia and hypoproteinemia. We cannot say what part the acute reduction in renal function that was associated with the acute obstruction of the ureter and the prolonged anesthesia played in this picture.

Oftentimes one sees a picture as that which follows: **Case 2.**—A man in good health had a five-hour anesthetic, and he reacted very well afterward. The total water intake for the first day was within normal limits, but the urinary output was low. The first day he passed only 200 cc. of urine. This oliguria was probably in greater part due to the prolonged anesthesia. The next day he passed 1500 cc. of urine, a mild diuresis that is commonly seen on the second day following ether anesthesia. However, in spite of this diuresis, there may not then have been enough urine put out in the first two days to care for the excretion of his phosphates and his sulphates, which have preferential rights of excretion over the chlorides, and so chlorides that may have been given in slight excess during these two days would tend to be retained.

The following day he became distended, began to vomit, and had liquid stools. (We find that saline retention is a very common cause of distention and of vomiting). His urine was now 400 cc., in spite of the fact that intake had been forced up. The following day he became irrational, and the salt and glucose solutions were greatly increased (5100 cc.–[2,500 of saline]) to cover the losses from the gastro-intestinal tract, with the result that his urine dropped down to almost nothing.

We then gave a liter of sodium lactate $\frac{M}{6}$, and within eight hours he had excreted 1150 cc. of urine, and 14 hours after the sodium lactate was given he was eating and drinking, and was fully rational.

There are seemingly two types of retention of fluids. We think that both of these stormy postoperative courses could have been avoided had we been more cautious in the use of the salt solution. I think I can give one or two rules that we are now following that enable us to avoid these complications which occur during the post-anesthetic period and occasionally in those who have not been operated upon—the anemic, the malnourished, and the nephritic.

Do not give salt solution unless there is a definite indication for its use. This means that the patient must have lost salt before you see him, *e.g.*, as a result of vomiting, diarrhea, fistula, sweating, *etc.* We prescribe it with the same care we prescribe any potent drug, such as digitalis or morphine. We think it is unwise to give salt solution for three days, at least, after operation, unless there is a very definite indication for its use. If salt solutions are to be given it is necessary that a nearly normal urine flow be established before the injection is begun. To establish a urine flow glucose solutions are used.

According to the very outstanding work of Wolfe, of the University of Rochester, it now looks as though, if one wishes to replace salt losses, it is wise to give salt solutions not as normal salt solutions but as solutions of five-tenths per cent or less.

Discussion.—Dr. Alfred Blalock (Baltimore, Md.): This paper of Doctor Coller, Doctor Moyer, and their associates, is an important one. It is rather disturbing to learn of the difficulties that one may encounter with the administration of normal salt solution.

A great deal of attention has been focused on the kidneys in recent years. All of us are familiar with the work on hypertension as produced by the Goldblatt method. Much interest has been displayed in the renal failure that may occur after crush injuries and after burns. In connection with crush injuries the most interesting recent comment is that of Bywaters, to the effect that one should ignore the shock that may appear early and should promote diuresis by giving large quantities of fluid before the renal blood flow is speeded up by the giving of plasma or blood. Now Coller and Moyer, and their associates add to the interest of surgeons in the kidneys by their important observations on the effects of anesthetic agents.

Although the kidneys are not very large organs, approximately one-fifth of the total cardiac output passes through them. Most tissues in the body react to a decreased blood flow by extracting increased portions of oxygen from the blood. Such is not the case with the kidneys unless the blood flow decreases greatly. In other words, the renal vein oxygen content remains high and the A–V difference small, except in dire emergencies. In other words, in shock the oxygen consumption of the kidneys is decreased much more than in most tissues. This may have something to do with the observations that have been reported today.

On the other hand, Moyer has stated that damage may occur in connection with anesthesia even when the renal blood flow and blood pressure are little if any affected. The explanation of their findings is not apparent. One would not expect anoxic anoxia to arise from the use of cyclopropane. Possibly, but not likely, histotoxic anoxia may be caused. It is possible that anesthetic agents produce harm by reducing the pulse pressure. Perhaps Doctor Moyer will comment on whether this occurs. As regards treatment, it is apparent that one should give a fluid such as glucose solution where the glucose could be metabolized and the water will be available for excretion by the kidneys.

Dr. Carl A. Moyer (Ann Arbor, Mich., closing): I will answer Doctor Blalock's question first. The decreases in glomerular filtration rate during cyclopropane anesthesia seemingly have little relationship to the systemic pulse pressures; decreases in filtration rate were noted with elevated as well as with lowered pulse pressures. In fact, diminutions occurred during periods that were characterized by an increased renal blood flow, an increased mean systemic blood pressure, and an increased pulse pressure.

We have no objective explanation for the above phenomenon. It is possible that intrinsic renal changes in capillary filtration pressure might have taken place that overshadowed the effects of the systemic elevation of pulse pressure and the increased renal blood flow. It is also possible that deformations in the various fluid compartments of the body that are incident to anesthesia might be responsible for some of the diminution in filtration rate. There is a mild hemoconcentration and a minor decrease in blood volume associated with cyclopropane and ether anesthesias; this would tend to decrease the effective glomerular filtration pressure provided that renal capillary pressure remained unchanged. Should the decreases in glomerular filtration rate that are associated with cyclopropane anesthesia (without hypotension) be due to the relatively small changes in osmotic pressure of the blood that are associated with anesthesia, it will be necessary to grant that the physical state of the blood that is being supplied to the kidney has more to do with the rate of glomerular filtration than has been suspected.

THROMBOSIS AND EMBOLISM*

REVIEW OF 202 PATIENTS TREATED BY FEMORAL VEIN INTERRUPTION

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THE RELATIONSHIP of venous thrombosis and pulmonary embolism has long been established. Postoperative pulmonary complications frequently ascribed to other causes have been due to infarct. The source of emboli has been generally considered mysterious, and often no sign of thrombosis was apparent prior to the fatal episode. This state of affairs has brought about an attitude of great fear concerning the possibility of sudden death during illness or following surgical procedures but has been accepted as an unavoidable sequence of events in a small percentage of cases. Although pulmonary embolism in the presence of well-defined thrombophlebitis has been understood, there have been many sudden deaths due to embolism, the source of which remained obscure. Gradually, there has come about a better understanding of the problem and the radical methods for reducing the morbidity and mortality.

Thrombophlebitis is apparently more common in some geographic localities than others. It seems that there is greater frequency of this disorder in New England than in the deep South. Perhaps this discrepancy is due to the same climatic variance commonly known regarding respiratory tract infections. Ochsner[1] has popularized the term "phlebothrombosis," which signifies a noninflammatory lesion. Homans[2] prefers the term "bland thrombosis," and both refer to a condition of venous thrombosis not associated with inflammation. This type is insidious in onset, produces little warning of pain, swelling, and fever, so that the condition is not suspected until infarct occurs. The thrombus in this instance is nonadherent to the vein and is easily dislodged. It is in these cases that we have our most serious problem and greatest number of deaths from pulmonary embolism. In true thrombophlebitis with pain, swelling, and fever, the thrombus is more or less fixed to the wall of the vein by the inflammatory process and although it is well known that embolism occurs in this variety, it is in fact less likely than in the nonadherent type.

Although the source of infarct and fatal embolus have been correctly supposed to come from the veins below the vena cava in thrombophlebitis, there has been a slow recognition of the fact that pulmonary embolism may occur in apparently well and afebrile patients. Pelvic veins have been accredited with the focus in many cases and often veins in the neighborhood of the

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wound have been suspected. Although infarcts may arise from these smaller veins, it is now believed that they are infrequently the source and never produce a sudden, massive fatal embolus. The heart has long been known to harbor thrombi, particularly in the auricles during or following fibrillation. Doubtless, a small percentage of fatal emboli do have their origin in the right heart.

Prettin[3] found that 133 out of 144 fatal emboli, studied by him, originated in the region drained by the inferior vena cava, and 91 of these patients had involvement of the femoral or iliac veins.

Hampton and Castleman[4] have demonstrated the clear-cut roentgenologic picture of infarct and have made it possible to diagnose this lesion with great accuracy. They have further shown that 95 per cent of all emboli exclusive of heart origin can be traced to the leg veins. These thromboses usually start in the veins of the calf muscles and propagate into the larger veins of the leg. The long, straight femoral vein can harbor enough thrombus to completely occlude the pulmonary artery if it becomes free at one time. Actually, repeated minor infarcts, or at least sublethal emboli, may precede, for several days and rarely for several weeks, a fatal episode.

MORBIDITY AND MORTALITY

Davis[5] studied the records of the Massachusetts General Hospital prior to 1925, and found that fatal pulmonary embolus occurred in three patients out of each 1000 subjected to operation. Miller and Rogers[6] found, in the same institution, that seven patients died of embolus out of 206 with clinical thrombophlebitis. Welch and Faxon,[7] in a later study, found the ratio of deaths to phlebitis to be about the same (1 to 25). They also found that one patient in three, with phlebitis, would have an infarct. Actually, the rate of fatal embolism has been reduced to one in each 800 operations performed in this institution. This reduction was brought about by a better understanding of venous stasis. Patients were encouraged, and actually aided, in frequent body exercises, deep breathing, and the leg veins kept empty by elevation of the foot of the bed. In spite of these safeguards, there continued to occur sudden deaths from massive embolus, many disabling infarcts, and much concern regarding the outcome in patients who developed thrombophlebitis. The morbidity in this group of cases was great. Many of the staff felt that a minimum of six weeks absolute bed-rest was imperative. It was found by Miller and Rogers that fatal embolus had not occurred in this group after the 27th day of the disease. One could never be sure when the process would involve the second leg, thus prolonging the hospital stay. Not only was this a painful, perilous period for all concerned but the patient often developed a permanent swelling in the affected leg, frequently resulting in postphlebitic ulcer.

Many attempts were made to improve the situation. Among these were the use of thyroid extract, heparin, leeches, and lumbar sympathetic block. Thyroid extract was given to the postoperative patients on one of the two

surgical services for a year, and at the end of this period no difference in the two groups was apparent. Leeches were difficult to manage but in a few instances of careful treatment of established thrombophlebitis by this method, the results were not spectacular. Heparin, with all its attended difficulties and cost, was amazing in its action when used according to the dictates of Murray.[8] Patients with thrombophlebitis on heparin would rapidly become afebrile and their legs symptomless. Since the action of this substance was not supposed to dissolve the original thrombus but prevent propagating thrombi, it was not surprising that difficulties concerning its use arose. Phlebitis would remanifest itself either in the original leg or its fellow after discontinuance of the drug. Infarcts took place after prolonged use of heparin, when it was stopped, and in one instance a fatal embolus occurred. We believe that heparin has its uses but need no longer be considered necessary in all cases. It is particularly helpful as a preventive measure in patients with a previous history of phlebitis, in patients who continue to have small infarcts after vein interruption, and as a preliminary to dicumarol administration. It may well be more effective in the treatment of bland thrombosis than in true thrombophlebitis. We are of the opinion however that simpler and safer methods are available.

Lumbar sympathetic block, first advocated by Leriche and Kunlin,[9] and popularized by Ochsner and DeBakey,[10] is a very useful procedure. The patient is more comfortable within a few minutes and morbidity is decreased. It is necessary to repeat the block with such frequency that many of our patients object strenuously to the necessary needle punctures of the lumbar region. We have come to look upon it as a valuable preliminary to more radical measures and use it occasionally in this manner. We feel that, as a therapeutic measure in the type of thrombophlebitis which we see, it is associated with too many disadvantages to warrant its complete adoption.

We have had too little experience with dicumarol to warrant any expression of opinion regarding it at this time. The drug has great possibilities in the prevention of thrombosis in suitable cases. Further safeguards are necessary before its use can be widely adopted.

Homans[11] is responsible for bringing to our attention the feasibility of interrupting the deep veins of the leg to prevent pulmonary infarction. Frund,[12] Bancroft, Stanley-Brown and Chargaff,[13] Taylor,[14] and Kulenkampf,[15] have all contributed articles of value to this phase of the subject. Welch, Faxon, and McGahey,[16] and Allen,[17] have published some of the experiences with this procedure from the Massachusetts General Hospital, and it is our intention in this report to analyse the material, up to January 1, 1943, from this institution.

There has been considerable pressure brought upon us by other departments in the hospital particularly by our medical colleagues. They feel that it is not possible to determine the source of infarct and that, since femoral vein interruption has been associated with no serious sequelae, we should undertake this procedure without hesitation. We have complied with this

request because the operation is simple and disturbs even seriously ill patients very little, and because we have found femoral and iliac vein thromboses in many of the cardiac patients who have had infarcts. We hoped that our analysis would make it possible to eliminate some of the obviously unnecessary interruptions and that we might set-up more clearly defined indications for the procedure.

Between 1937 and January 1, 1943, we have interrupted the femoral vein or veins in 202 patients. Bilateral operations, either at the same time or at subsequent dates, bring the total deep veins interrupted to 280 (Table I). The tremendous increase from 55 interruptions in 1941 to 211 in 1942 is due to increased confidence in the procedure and to an increase in the number of bilateral operations.

TABLE I

NUMBER OF FEMORAL VEIN INTERRUPTIONS IN 202 PATIENTS

Massachusetts General Hospital

(According to Year)

1937	1
1938	0
1939	8
1940	5
1941	55
1942	211
Total	280

The sex ratio is surprising, in that we find that 126, or 62 per cent, of the patients operated upon are males. We had expected that, inasmuch as thrombophlebitis was more common in the female, bland thromboses would also prove more common in this sex. In this institution, the sex ratio of patients is almost equal.

TABLE II

AGE OF PATIENTS IN DECADES

202 CASES OF THROMBO-EMBOLIC DISEASE

Massachusetts General Hospitaal—1937-1942 (Incl.)

0-10	1	0.5%	
10-20	4	2%	19%
20-30	9	4%	
30-40	24	12%	
40-50	37	18%	
50-60	53	26%	81%
60-70	49	24%	
70-80	25	13%	
Total	202		

The age distribution is important (Table II). We knew that fatal embolus was rare in the young patient and that the danger of this complication was in a direct ratio to the patient's age, from a study of this phase of the subject made in our clinic by Welch and Faxon.[7] We are, therefore, not surprised to find that 81 per cent of the patients receiving femoral vein interruption were over forty years of age. One may well ask why the operation was undertaken in the younger age-group at all. The reasoning

is logical, since the operation is simple; it protects the patient from the added morbidity of pulmonary infarcts and the prolonged hospital stay from the venous thrombosis and also eliminates the chance of a rare fatal embolus.

TABLE III

ANALYSIS OF 202 CASES THROMBO-EMBOLIC DISEASE TREATED BY FEMORAL VEIN INTERRUPTION

Massachusetts General Hospital—1937-1942 (Incl.)

Number of veins interrupted:				
Right common femoral	27		20%	
Right superficial femoral	103		80%	
Total (right)		130		46%
Left common femoral	39		25%	
Left superficial femoral	111		75%	
Total (left)		150		54%
Total		280		
Number of unilateral operations	124		61%	
Number of Bilateral operations	78		39%	

An analysis of the veins interrupted is shown in Table III. We had supposed that there would be a greater number of left veins operated upon since there has been some statistical data on an anatomic basis to support a greater frequency of thrombophlebitis in the left leg veins. Our tendency to increase the number of bilateral ligations may have influenced these figures. The location of interruption above or below the profunda femoris vein may be of little importance, although we have contented ourselves with the superficial femoral vein in from 75 to 80 per cent of the cases. We thought this procedure would result in a shorter period of postoperative edema; and, occasionally, even in the presence of profunda femoris thrombosis, we have not always interrupted the common femoral. Actually, when one removes the thrombi by suction from the iliacs, it may make little difference where the vein is ligated and divided; usually, however, if the profunda is thrombosed, the interruption has been above it. It is quite likely that some of the rare infarcts, that occurred after superficial femoral interruption, may well have come from the profunda vessels.

TABLE IV

INDICATIONS OF VENOUS THROMBOSIS

No. of cases with chest pain as first symptom	82	41%
No. of cases with leg signs as first symptom	120	59%
No. of cases with suitable charts for study	74	
No. of cases with positive clinical chart noted	60	81%
No. of extremities examined for swelling	237	
No. of extremities showing swelling	159	67%
No. of extremities examined for tenderness	231	
No. of extremities showing tenderness	143	61%
No. of extremities examined for Homans' sign*	139	
No. of extremities showing positive Homans' sign	59	42%

*Homans' sign is a term used in our clinic. Dr. John Homans calls it the dorsiflexion sign. It is carried out by dorsiflexion of the foot with the knee straight. If the patient complains of pain or soreness in the calf muscles when this is done the sign is interpreted as positive for venous thrombosis.

Indications for femoral vein interruption are shown in Table IV. Fifty-nine per cent of the cases had leg signs or symptoms as the first indication of trouble, while 41 per cent had chest pain first. This undoubtedly explains the fact that there has been an occasional fatal embolus during an otherwise apparently normal convalescence, in spite of our alertness regarding bland thrombosis. When the clinical chart shows an elevation of temperature, pulse, and respiration, one should examine the patient's legs with utmost care and if minimal signs are noted, proceed with bilateral femoral vein interruption. We regret to say that, due to the difficulty in maintaining a four-hourly chart, many of these early warnings are missed. Also, we believe it is important to have an elevation of temperature, pulse, and respiration together, since one or two of them may be elevated while the second or third, or both, may be unchanged.

Phlebography appeared to be the solution to the question of a reliable indication for vein interruption. Welch, Faxon, and McGahey[16] became expert in the technic and interpretation of the films and felt, at the time of their publication, that it was a reliable and desirable method of procedure.

TABLE V

PHLEBOGRAMS

Positive with positive clinical findings	55		67%
Negative with positive clinical findings	27		33%
Total		82	
Positive with negative clinical findings	19		41%
Negative with negative clinical findings	27		59%
Total		46	
Positive with pulmonary emboli	33		49.3%
Negative with pulmonary emboli	34		50.7%
Total		67	
Positive phlebograms	78		54%
Negative phlebograms	67		46%
Total		145	
No. femoral veins interrupted—1941		53	
No. phlebograms—1941		36	68%
No. femoral veins interrupted—1942		211	
No. phlebograms—1942		104	50%

Table V shows the exact experience we have had with phlebograms. There is a definite trend to rely upon this test less as time goes on. The finding of positive clinical evidence of thrombi with negative phlebograms in one-third of the cases makes us feel that only in very doubtful or borderline cases is phlebography indicated. Furthermore, the ideal time to interrupt the femoral vein is when the venous thrombosis is still localized to the lower leg, and it is in these cases that phlebography is most difficult to interpret. We have come to depend on the clinical examination and believe that phlebography will be used less during the present year than in the past in our clinic.

The reliability of our decision for venous interruptions in the 202 patients operated upon are indicated in Table VI. In patients with infarcts, 35.7 per

TABLE VI

202 PATIENTS WITH FEMORAL VEIN INTERRUPTION

	Thrombi Found at Operation	Thrombi *Not* Found at Operation	
Patients with infarcts	30	54	35.7%
Patients without infarcts	56	62	47.4%

cent still had thrombi in the veins, while in those operated upon before infarct occurred, 47.4 per cent had thrombi. This we believe is significant and shows probably that the diagnosis of thrombosis should be followed by venous interruption before infarct takes place, if possible. The negative explorations mean that the thrombus, or a portion of it, has either left the vein or is still in the lower veins of the leg.

During 1942, many vein interruptions were undertaken upon patients with symptoms localized to the lower leg, and in this group thrombosis of the femoral vein is not expected. Our present opinion is that, if possible, the operation should be carried out before thrombosis has extended into the femoral and iliac veins. As our diagnostic acumen improves in detecting early thrombosis, the number of negative explorations will increase, yet the protection afforded by the operation is not diminished.

TABLE VII

MORBIDITY STATISTICS IN CASES OF THROMBO-EMBOLIC DISEASE TREATED BY VEIN INTERRUPTION

Massachusetts General Hospital—1937-1942 (Incl.)

I. Days after vein interruption to flat chart:	
No. of cases	162
Average no. of days	4.5
II. Days after ligations to discharge from hospital:	
No. of cases	84
Minimum no. of days	3
Maximum no. of days	13
Average no. of days	8.4

Table VII gives an idea of the morbidity following femoral vein interruption. It is to be noted that only 162 cases were available for the study of the clinical chart, while only 84 patients could be evaluated on the basis of hospital stay. These are not selected however, and we believe represent a true picture of the situation. Obviously, it was not fair to include in these data, the records of patients remaining in the hospital for heart disease or for the treatment of fractures or complicated surgical procedures, nor was it reasonable to include the clinical charts that were affected by the patients' primary lesion. We wish to confirm by these data only the impression that we have acquired a rapid return to health after femoral vein interruption, and an early discharge from the hospital. When one compares these figures with those available for any other method of treatment used for thrombophlebitis, it is evident that the morbidity is tremendously reduced by venous interruption.

Table VIII brings out some interesting data. The majority of the infarcts occur in the lower lobes of the lungs, and the left lower lobe is more frequently involved than the right.[19] This is thought to be due to the

TABLE VIII

LOCATION OF PULMONARY EMBOLI

Left lower lobe	66	69.5%
Right lower lobe	41	36.9%
Left upper lobe	3	2.7%
Right middle lobe	0	0
Right upper lobe	1	0.9%

anatomic arrangement of the pulmonary circulation, and the fact that the blood flow is more rapid through the lower than the upper lobes. An embolus, for this reason, will be carried by the swiftest current to lodge most frequently in the left and right lower lobes. The rarity of embolism of the upper lobes may be of value in ruling out pulmonary embolism when a questionable lesion is found in that part of the chest.

There were, as we expected, a few infarcts after femoral vein interruption. Eleven of the 202 patients had this complication. Two of these patients died after leaving the hospital. One in Case 7 in the analysis of deaths, and may well have had a fatal embolus from the uninterrupted vein on the opposite side. He was a cardiac, and could well have succumbed to heart disease. The other patient died suddenly at home, one month after discharge from the hospital. She had had bilateral superficial femoral interruption, and no thrombi were found at this level. At autopsy, some thromboses were found in the pelvic veins but the fatal embolus was found to have arisen in the right auricle. The other nine patients in this group recovered; four of them were cardiacs. One patient, who had infarcts after prostatectomy, continued to have emboli following bilateral superficial femoral interruption for positive leg signs. He was given heparin for eight days and recovered. Eight of these 11 patients had bilateral interruption. In retrospect, it seems probable that the convalescence could have been shortened in the two survivors who had unilateral operations.

TABLE IX

CARDIAC PATIENTS WHO HAD FEMORAL VEIN INTERRUPTION*

Positive leg signs with clots	4
Positive leg signs without clots	10
Negative leg signs without clots	5
Positive phlebograms with clots	1
Negative phlebograms without clots	8

*All in this group had infarcts or definite signs of phlebitis. Infarcts were doubtless cardiac in origin in some instances.

In the cardiac group (Table IX), we find that in five patients with negative leg signs, no thrombi were found in the veins at operation; on the other hand in ten patients with positive leg signs and in eight with positive phlebograms, no thrombi were found in the femoral veins. One immediately wonders if the absence of thrombi at this level could be interpreted on the basis of thrombi in the veins above this region. In most instances, however, in this group, femoral vein interruption was undertaken on mimal evidence of thrombosis involving the veins of the lower leg, so that it was not expected to find thrombi in the femoral vein. The fact that the femoral vein is opened and free bleeding obtained from both direc-

tions is, in our opinion, evidence that any thrombosis that exists would of necessity be in the smaller veins of the pelvis or of insufficient size to interfere with blood flow through the main veins. We are willing to accept the more likelihood of infarct from cardiac origin in most of these cases.

Patients, who died of their disease and who had been subjected to femoral vein interruption, are analysed in Table X. There are 12 in this group, two of them dying after discharge from the hospital, and are mentioned above. All of these patients, we feel sure, succumbed to causes unrelated to femoral vein interruption. Perhaps, one patient died from embolus originating in the uninterrupted vein in the opposite leg. It is surprising to us that such an outcome has not occurred in others in our group. We have, in nearly every instance, interrupted the vein on all legs that have given us positive clues of involvement. As a matter of fact, we have found thrombosis in so many supposedly normal extremities that we are inclined to feel that simultaneous routine interruption of the opposite vein should be undertaken.

SEQUELAE

Sequelae following femoral vein interruption have been surprisingly few. Actually, postoperative edema is the most serious of these, and there has been so little complaint on the part of the patients regarding this that it is relatively unimportant. In Table XI, we have tried to bring this out. We were particularly interested in determining, if possible, the difference in edema in superficial and common femoral interruption. It appears that early swelling is more frequent after common femoral interruption but late edema seems to be about the same in both groups. The average patient wears a woven bandage for three to four weeks after discharge and then abandons it as unnecessary. A few are more comfortable with supports for long periods of time. There seems to be less swelling in these extremities than one usually sees following a spontaneous recovery from thrombophlebitis. So far, we have observed only one transient ulcer of the postphlebitic type in this group.

Homans feels that there will be less subsequent edema if the common iliac is divided rather than the femoral. He has anatomic evidence to support this view on the basis of a greater number of contributory veins coming in between the levels of the femoral and iliac veins.

In old cases of thrombophlebitis with infarct, one may do well to interrupt the venous circulation at a higher level. It is usually impossible to remove these old, inflammatory, adherent thrombi through an incision in the femoral vein. Doubtless, it is better to interrupt the vein above the thrombus if it cannot be removed. Homans[2] prefers to ligate the common iliacs through a long oblique ureteral incision retroperitoneally—the right common iliac vein is quite easily exposed by this route. The left vein lying behind and to the right of the artery is more difficult to approach. He has reported six right and six left iliac vein interruptions.

The feasibility of interruption of the vena cava in continuity through

TABLE X

ANALYSIS OF DEATHS

Case		Age	Sex	Diagnosis	Operation	Veins* Interrupted	Clot Found	Pulmonary Emboli: Before Oper.	Pulmonary Emboli: After Oper.	Days of Disease to Ligation of Vein	Autopsy	Condition of Veins: Clot Below Lig.	Condition of Veins: Clot Above Lig.	Emboli: Old	Emboli: New	Cause of Death	Days from Lig. of Vein to Death
1.	W. C.	65	M	Glaucoma art' scl. heart dis.	Eye operation	L. S. F.	0	+	0	21	+	+	0	+	0	Cardiac failure	11
2.	M. P.	66	M	Ca. of stomach	Subtotal gastrectomy	L. S. F.	0	0	0	1	0	—	—	—	—	Peritonitis	2
3.	A. M.	62	M	Ca. of colon	Resection of colon	R. S. F. L. S. F.	0 0	0 0	0 0	1	0	—	—	—	—	Recurrent ca. Intestinal obst.	 52
4.	J. G.	45	M	Ca. of bladder	Uret.-enterost. rt. nephros.	R. C. F.	+	+	0	2	+	+	+	+	0	Sepsis about right kidney	10
5.	A. C.	62	M	Ca. colon. Acute cholecy., c bile periton.	Right colectomy	R. S. F. L. C. F.	0 +	0	0	1	+	0 +	0 +	0	0	Bile peritonitis	 7
6.	T. L.	52	M	Coronary heart dis.	None	R. S. F.	0	+	0	245	+	+	0	+	0	Coronary infarct	28
7.	A. R. S.	39	M	Coronary heart dis.	None	L. S. F.	0	+	0	4	0	—	—	—	—	Coronary heart dis.	15
8.	M. B. S.	69	F	Coronary heart dis.	None	L. S. F.	0	+	0	27	+	+	0	+	0	Coronary heart dis.	27
9.	H. H.	79	M	Sprained ankle	None	R. C. F.	+	0	0	7	+	+	+	0	0	Pneumonia	30
10.	B. E.	39	F	Ca. of uterus	None	L. C. F.	+	0	0	3+	+	+	+	+	0	Uremia	8
11.	G. G. R.	52	M	Dermatomyositis	None	R. C. F. L. C. F.	+ +	0	+	27	+	+ +	+ +	+	+	Dermatomyositis	 3
12.	C. S.	40	F	Rheumatic heart dis.	None	R. S. F. L. C. F.	0 0	+	+	10	+	0 0	0 0	+	+	Mult. infarcts	49

*R. & L. S. F.—Right & Left Superficial Femoral Vein.
R. & L. C. F.—Right & Left Common Femoral Vein.

a right loin incision, similar to that used in lumbar sympathectomy, has been demonstrated by one of us.[18] This is certainly the procedure of choice if bilateral iliac interruption was indicated.

The total salvage from femoral vein interruption is enormous. Although it may not be possible to prevent all deaths from massive bland thrombi, the possibility must be kept constantly in mind, so that minor signs and symptoms will not escape our attention. On the other hand, the morbidity saving is unquestionable and tremendous. One may decide to attempt preventive vein interruptions in certain predisposed, or elderly, individuals. This seems to us difficult at the moment, since prediction regarding such complications is unreliable in the light of our present knowledge.

TABLE XI

POSTEPERATIVE EDEMA FOLLOWING FEMORAL VEIN INTERRUPTION

Massachusetts General Hospital—1937-1942 (Incl.)

	Number of Cases	Number With		Number Without	
IMMEDIATE EDEMA					
Right common femoral	19	13	70%	6	30%
Left common femoral	34	29	85%	5	15%
Total	53	42	80%	11	20%
Right superficial femoral	78	37	47%	41	53%
Left superficial femoral	82	39	48%	43	52%
Total	160	76	47.5%	84	52.5%
LATE EDEMA					
Right common femoral	6	2	33%	4	67%
Left common femoral	20	10	50%	10	50%
Total	26	12	46%	14	54%
Right superficial femoral	26	8	31%	18	69%
Left superficial femoral	31	16	52%	15	48%
Totals	57	24	42%	33	58%

OPERATIVE TECHNIC

The operation of femoral vein interruption as carried out in our clinic is as follows: The patient is operated upon with a slight elevation of the trunk to insure positive venous pressure from above. Novocain infiltration anesthesia is used. The incision is guided by the pulsation of the femoral artery in the groin and extends distally three inches in the direction of the vein. We believe this allows a better retraction of the lymphatics and a minimal division of them—this offsets the advantage of an oblique incision making for a fine scar. The femoral sheath of the vascular bundle is divided longitudinally and the artery retracted laterally. The vein is exposed over a distance of two inches in the center of the vertical skin incision. This brings into view the common, superficial, and deep femoral veins, which are freed sufficiently to allow a ligature to be placed under them. These ligatures are left untied and used to control bleeding after the vein is incised. If the common femoral appears thrombosed, it is opened; if it appears uninvolved, the superficial femoral is opened. The incision

in the vein is made transversely and through only the anterior half. Thrombi extrude through the incision and are withdrawn from the upper segment first. Suction, carefully applied, through an angulated glass drinking tube, which is inserted through the vein incision into the iliac, frequently makes it possible to clear the proximal segments sufficiently to allow free bleeding. After this is accomplished, the lower segment is cleared of thrombus by the same method. The introduction of the aspirating cannula proximally has never dislodged a thrombus. The previously placed ligatures are then tied and the vein completely divided. Transfixion sutures distal to the ligatures are then used. The wound is washed out with salt solution and closed without drainage.

The entire procedure requires about 30 minutes. In the inflammatory veins, the patient feels slight discomfort during the manipulation of the vein. Patients are allowed out of bed as soon as they become afebrile or their general condition permits. This is often on the day following the removal of a bland thrombus. We have rarely been troubled with a short period of lymph drainage through the wound.

SUMMARY AND CONCLUSIONS

1. Femoral vein interruption for the prevention of pulmonary embolism is a simple, safe operative procedure and can be carried out upon very ill patients.

2. The indications are usually apparent. Pulmonary infarcts, tenderness over the leg veins, swelling of the leg—however slight, dilated superficial veins, discomfort in the calf muscles if the foot is passively dorsiflexed (Homans' sign), and slight elevation of the temperature, pulse, and respiration, are all satisfactory guides. One usually has to make a decision on one or two of these criteria, although frequently all are present.

3. Phlebograms are difficult to interpret and may be misleading.

4. In a large majority of cases, bilateral interruption should be undertaken. Unilateral interruption may be safely done as the indications arise in the younger age-group. In patients beyond the age of forty, bilateral interruption at one sitting should be the rule.

5. We are sure that mechanical removal of the thrombus from the vein by aspiration is a safe procedure. It certainly reduces the pain and swelling in the leg, and hastens recovery.

6. No deaths have occurred in a group of 202 patients as a result of femoral vein interruption.

7. Sequelae are not severe and they are not disabling.

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PEROXIDE OINTMENTS*

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THE VALUE OF PEROXIDE THERAPY has become established in recent years for a variety of surgical conditions. We are indebted principally to Meleney, and his associates,[1, 2, 3, 4, 5, 6, 7, 8, 9] for their demonstrations of its capabilities in the treatment of progressive bacterial synergistic gangrene, chronic undermining burrowing ulcers on all parts of the body surface, gas gangrene and tetanus after excision of involved tissues, fusosphirochaetal infections of the mouth and neck and human bites infected with these organisms, chronic ulcerations of the vagina, perirectal and deep pelvic abscesses, diabetic infectious gangrene, amebic infection with gangrene, lung abscess, actinomycosis, and other malodorous infections. It has also been described in the treatment of decubital ulcers,[10] foul smelling infected malignant lesions and radionecrotic ulcers by a number of authors.[11, 12, 13] The effectiveness of zinc peroxide in arresting the continued hemorrhage complicating chronically infected burns after all other forms of therapy that had been tried had failed was reported from this clinic[14] one year ago.

It has also been used postoperatively as a prophylactic dressing for recent accidental wounds[15, 16] and for wounds resulting from operations for fecal fistulae, pilonidal sinuses and rectal and colonic lesions.

More specifically, peroxides are indicated principally in the care of wounds or other lesions caused, or secondarily infected, by anaerobic streptococci, microaerophilic hemolytic and nonhemolytic streptococci, *Cl. tetani,* anaerobes of the gas gangrene group, *B. melaninogenicum, B. fusiformis,* Actinomyces, and certain Spirochaetes.

In the past, peroxide therapy has been limited largely to the use of hydrogen peroxide irrigations or the daily application of a water suspension or cream of zinc peroxide. The chief disadvantage of hydrogen peroxide is the rapidity with which all of its oxygen is dissipated on a wound surface, necessitating frequent or continuous irrigation by this solution. Although zinc peroxide suspended in water has been found to be very effective therapeutically, it has certain disadvantages which tend to limit its use to large and well-equipped hospitals:

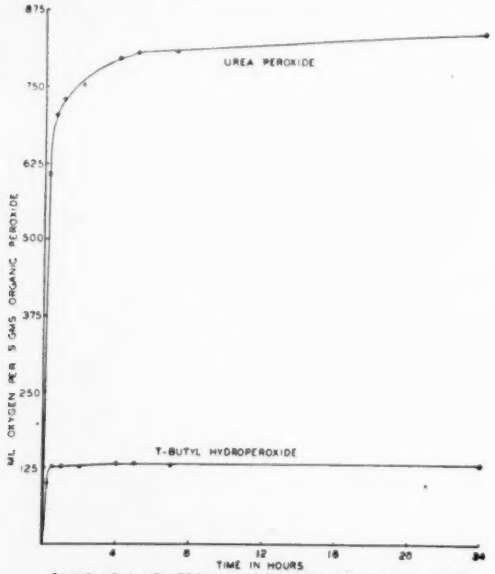
1. The physical activation of the zinc peroxide powder requires its heating for four hours in a carefully regulated dry oven.

2. The suspension must be freshly and correctly made before each dressing since it will not keep, an obvious disadvantage on a busy ward, in the home, or the office.

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

3. Daily dressings are required because the oxygen is usually dissipated in the wound in 24 hours or less.

4. Suspensions of zinc peroxide and the oxide and hydroxide which it forms have a tendency to congeal as flakes or concretions which may be difficult to remove without causing pain or bleeding from the depths of a wound. If allowed to remain in the wound for any length of time they may excite a local foreign body reaction.



OXYGEN EVOLVED FROM UREA PEROXIDE AND T-BUTYL HYDROPEROXIDE IN CONTACT WITH SHEEP PLASMA AT 37°C

FIG. 1

It is our impression that the field of usefulness of peroxide therapy would be definitely extended if one or more active and stable peroxide ointments were generally available. Until the present most attempts to produce an active and stable ointment have failed principally because of the lack of a suitable ointment base. In our experience as well as in that of Meleney,[17] the ordinary grease ointment bases greatly decrease the activity of zinc peroxide, while greaseless bases or vanishing creams containing zinc peroxide permit satisfactory evolution of oxygen if used immediately, but do not make stable ointments.

During the past one and one-half years, we have studied the problem of producing an active and stable peroxide ointment in association with the Research Division of the William S. Merrell Company. Our first efforts were directed toward the development of a suitable base. A satisfactory base had to be water-soluble yet contain or absorb no water on standing. It had to have a melting point at body temperature, so that its application would be followed by the filling of all the recesses and depths of the wound, insuring intimate and continued contact with these surfaces. Such a base

was found in the solution of "Carbowax"-1540 by one of several glycol diluents such as hexaethylene glycol-polyethylene glycol-300 or nonethylene glycol-polyethylene glycol-400. The proportions of these constituents used can be varied according to the amount and type of peroxide to be used. The "Carbowax" and the glycols are produced by the carbide and Carbon Chemicals Corporation of New York City. "Carbowax"-glycol ointment base used on experimental and human wounds is nontoxic and does not appear to alter perceptibly the rate of wound healing.

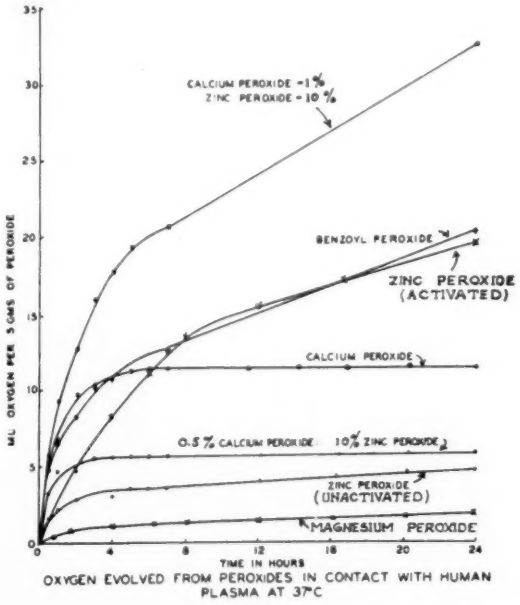


FIG. 2

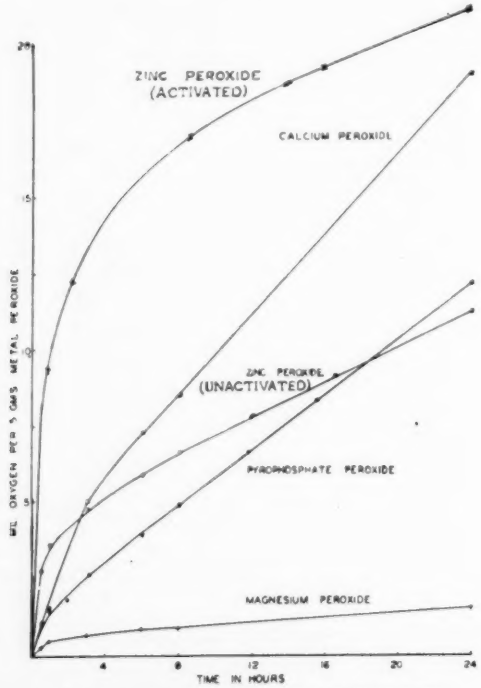
Using the "Carbowax"-glycol base it is possible to make a suitable ointment with zinc peroxide. It is significant that Meleney, working independently and at about the same time, also decided upon "Carbowax" as the most satisfactory ointment base for zinc peroxide. After considerable experimentation with different combinations of "Carbowax" and the various glycols, a satisfactory zinc peroxide ointment was developed having the following formula:

"Carbowax"-1540 ..... 120 Gm.
Nonethylene glycol-polyethylene glycol-400... 80 cc.

These are mixed thoroughly in a boiling water bath until dissolved. To the cooling solution is added 10 per cent finely milled, activated zinc peroxide and 0.2 per cent of cetyl pyridinium chloride which are stirred continually until a smooth homogeneous ointment is formed.

Other glycols such as hexaethylene glycol-polyethylene glycol-300 can be used satisfactorily with the "Carbowax" by varying the proportions. Merck's or Mallinckrodt's medicinal grade of zinc peroxide should be used,

and activated by heating to 140°C. for four hours in a dry oven for best results, although a less effective ointment can be prepared from the unactivated material. Cetyl pyridinium chloride is a wetting agent as well as an effective antiseptic, and the addition of 0.2 per cent of this substance increases the amount of oxygen released by zinc peroxide by approximately 20–25 per cent. This ointment is yellowish-white in color, moderately greasy in consistency, has a melting point of 38–39°C., and a p_H of 7.2. If lanolin is added to the above formula, the evolution of oxygen from the zinc peroxide is decreased 27 per cent.



EVOLUTION OF OXYGEN FROM PEROXIDES IN CONTACT WITH WATER AT 37°C.

FIG. 3

This ointment will release oxygen when coming in contact with water, serum, plasma, perspiration, or wound secretion. This is important, in that oxygen will be evolved from zinc peroxide in an open wound or lesion without the addition of water, the reaction apparently being dependent upon peroxidase present in the secretions. The greater the effusion of wound juices, the greater the release of oxygen over a 24-hour period and, under some conditions, a three- to four-day period (Fig. 1). During its decomposition in water this ointment has a p_H of 9.55, and in plasma a p_H of 9.4

To test the stability of this ointment, samples were stored at 37°C. for six months (high above the average room temperature). Under such conditions the ointment held up well, and the total amount of oxygen evolved

from a five Gm. sample of ointment decreased only 6.5 per cent after two months, and only 15.2 per cent after six months. The rate of oxygen released after this period of storage follows the same general curve as that of the freshly prepared ointment. It is to be remembered that the decomposition of zinc peroxide powder is much more rapid during the first month after its activation.

Our clinical tests with this ointment over the past eight months have been satisfactory. The technic employed in dressing a granulating wound, or other lesion, consists of preliminary gentle cleansing of the surface with

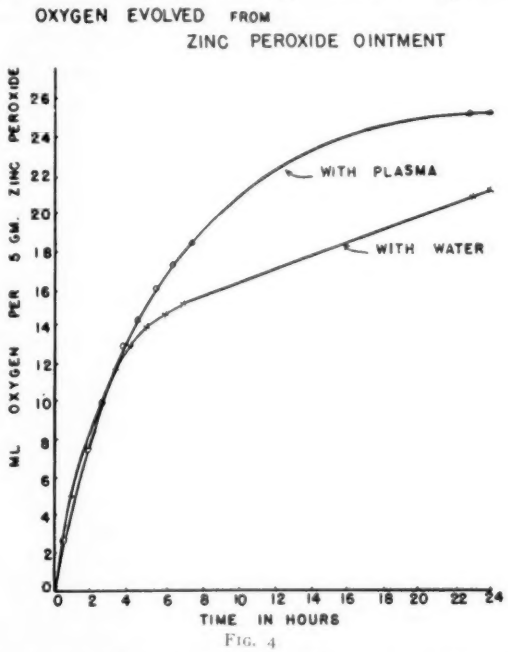


FIG. 4

hydrogen peroxide and saline solution, followed by the liberal application of the ointment to insure complete, intimate and lasting contact with all parts of the lesion. The low melting point of the base facilitates this. Since the zinc peroxide is gradually decomposed by wound secretions or plasma, it is not necessary to add water, or to cover the ointment with gauze or cotton pads soaked in water, although we have usually done this. A layer of vaseline or zinc oxide ointment gauze is then used to cover the area and seal in the evolved oxygen and the wound secretions. The interval between dressings may be 24 to 72 hours, but our experience indicates that it should never be as long as five or more days because of the reaction the residue, namely, zinc oxide and zinc hydroxide, may produce in the wound. In such cases a marked increase in the amount of purulent exudate may occur and this exudate may also become bloody. We have thought that this was the result of a foreign body reaction produced by the zinc oxide and zinc hydroxide residue.

If the proportion of "Carbowax" is increased and that of the glycol is decreased, a satisfactory base is obtained for making zinc peroxide vaginal or rectal suppositories.

Other peroxides have been studied to see if any was superior to zinc peroxide for peroxide therapy. Two main groups of peroxides were available for this purpose, the inorganic and the organic. The inorganic group contained metallic radicals and consisted of zinc peroxide, calcium peroxide, sodium pyrophosphate peroxide, and magnesium peroxide. The organic group consisted of urea peroxide, benzoyl peroxide, benzyl peroxide and tertiary butyl peroxide.

APPARATUS AND PROCEDURE FOR STUDYING THE EVOLUTION OF OXYGEN FROM PEROXIDES

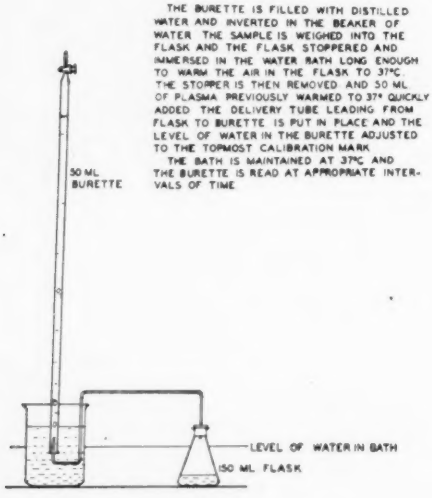

THE BURETTE IS FILLED WITH DISTILLED WATER AND INVERTED IN THE BEAKER OF WATER. THE SAMPLE IS WEIGHED INTO THE FLASK AND THE FLASK STOPPERED AND IMMERSED IN THE WATER BATH LONG ENOUGH TO WARM THE AIR IN THE FLASK TO 37°C. THE STOPPER IS THEN REMOVED AND 50 ML OF PLASMA PREVIOUSLY WARMED TO 37° QUICKLY ADDED. THE DELIVERY TUBE LEADING FROM FLASK TO BURETTE IS PUT IN PLACE AND THE LEVEL OF WATER IN THE BURETTE ADJUSTED TO THE TOPMOST CALIBRATION MARK.
THE BATH IS MAINTAINED AT 37°C AND THE BURETTE IS READ AT APPROPRIATE INTERVALS OF TIME
50 ML BURETTE
LEVEL OF WATER IN BATH
50 ML FLASK

FIG. 5

The inorganic peroxides are insoluble in water but are decomposed gradually at a sustained rate by water, blood, plasma, and wound secretions, giving off comparatively small quantities of oxygen and leaving a residue. The organic peroxides tend to be soluble in water and are decomposed rapidly by plasma, leaving no insoluble residue. Water, however, causes very little release of oxygen.

To study the evolution of oxygen from the various peroxides, a simple but effective apparatus was devised by the Merrell Research Laboratories, which is depicted and described in Figure 2. The rate and amount of oxygen released by the inorganic peroxides in the presence of water at 37°C. was measured, and is illustrated graphically in Figure 3. Zinc peroxide after preliminary activation by heat produces the greatest amount of oxygen at a sustained rate. If unactivated, the amount of oxygen released is reduced 60 per cent. The curve produced by calcium peroxide is very satisfactory while those by sodium pyrophosphate peroxide and unactivated zinc peroxide are similar

to each other. The small amount of oxygen released by magnesium peroxide makes it obviously not suited for this purpose.

A comparison of the evolution of oxygen from the various peroxides in the presence of human plasma at 37°C. is shown in Figures 4 and 5. The rate and amount of oxygen released by activated zinc peroxide in the presence of plasma is very similar to that released in the presence of water, while magnesium peroxide, unactivated zinc peroxide and calcium peroxide give off very small amounts of oxygen. The curve of benzoyl peroxide is very similar to that of activated zinc peroxide, but its highly explosive and inflammable nature precludes its use topically for clinical purposes. Urea peroxide and T-butyl hydroperoxide both release much larger quantities of oxygen than activated zinc peroxide, but the evolution is so rapid that it is complete in four to eight hours, an obvious disadvantage.

Ointments may be prepared with each of the above peroxides using the "Carbowax"-glycol base. The inorganic peroxide ointments can be made stable, but the organic tend to be unstable. Urea peroxide ointment, if carefully made will remain stable.

The p_H of the various peroxide ointments in the presence of water and plasma is shown in Table I, as determined by the Leeds and Northrop glass electrode potentiometer.

TABLE I

	ZnO_2 10%		CaO_2 10%		MgO_2 10%		Urea Peroxide		T-Butyl Hydro-Peroxide	
	H_2O	Plasma	H_2O	Plasma	H_2O	Plasma	H_2O	Plasma	H_2O	Plasma
5 mins.....	7.2	9.3	12.0	11.0	10.0	9.75	3.30	5.90	4.68	6.5
4 hrs.....	9.55	9.4	11.24	11.05	9.9	9.86	4.20	5.75	3.9	6.8
24 hrs.....	9.30	9.74	11.95	11.13	10.06	10.10	3.35	5.66	4.14	6.5

The results are very interesting. It will be noted that the inorganic peroxides produced an alkaline reaction in the presence of either water or plasma, while the organic ones gave strongly acid reactions. The low p_H given by urea peroxide and T-butyl peroxide and the high p_H produced by calcium peroxide indicate the irritant nature of these substances when applied to wounds or other lesions. Plasma has a buffering action which decreases to a certain extent the acidity or alkalinity of these preparations.

Our clinical investigations have been limited to the use of zinc peroxide and urea peroxide ointments. Zinc peroxide ointment has proven satisfactory when used for specific indications, as described by Meleney. We have noticed rapid control of infection and disappearance of foul odors with no apparent delay in wound healing. If the zinc peroxide dressing was not changed at least every two or three days, and the residue was allowed to remain on the surface of a raw or granulating wound for a period of five or more days, a marked increase in bloody purulent exudation occurred, presumably from the irritant action of this foreign body. With three percent urea peroxide ointment, more frequent change of dressings were necessary since the rate of oxygen evolution was rapid and unsustained. Its

use on infected wounds containing considerable slough was usually followed by rapid control of infection and separation of the necrotic tissue. Although urea peroxide does not leave an insoluble residue in the wound and although it may have a synergistic effect with sulfanilamide, our repeated observations show it has three very serious disadvantages: Its local irritant action; a marked delay in wound healing occurring with its continued use; and its sudden unsustained release of oxygen. The rapid evolution of oxygen produced by urea peroxide ointment makes it an effective prophylactic agent for lewisite burns. Our experiments have shown that application of this ointment to the skin as long as ten minutes after exposure to lewisite vapor or liquid will either entirely prevent or greatly diminish the size and severity of the local lesion.

SUMMARY AND CONCLUSIONS

The value of active and prophylactic peroxide therapy has become established for a variety of surgical conditions. For most effective use, peroxide therapy should not be employed indiscriminately but should be used intelligently and be limited to specifically indicated conditions. It is our belief that treatment by Dakin's solution is still the most satisfactory therapy for the majority of infected granulating wounds or lesions seen by the surgeon.

From our studies, it is obvious that the ideal peroxide for local therapeutic use has not been found as yet. Each peroxide investigated has its disadvantages, but of those studied, zinc peroxide still seems to be the most effective and satisfactory. Its chief advantages are safety and durability of action.

Certain disadvantages of using water suspension of zinc peroxide tend to limit its use to large and well-equipped hospitals. To overcome many of these disadvantages and to extend the field of usefulness of peroxide therapy, an active, effective, and stable zinc peroxide ointment has been developed.

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DISCUSSION.—DR. FRANK L. MELENEY (New York): Doctors Altemeier and Reid have made an important contribution to the study of surgical infections, as their report clearly indicates. There have been very real difficulties in the clinical use of zinc peroxide powder suspended in water. The chief disadvantage is that it must be kept moist in order to have it remain active in its oxygen evolution and in order to prevent mechanical irritation of the wound if it dries up. This disadvantage may be obviated by covering the innermost dressing (which may be either a thin layer of cotton or fine-mesh gauze) with an outer layer of cotton soaked in water, which is then sealed over with a rubber sheet, if it is a flat surface, or with zinc oxide ointment-impregnated gauze, if it is a curved surface. One great advantage of this dressing is that it can be removed very readily and is never adherent to the wound if it remains moist. If properly sealed it will remain moist for 48 hours. If the zinc peroxide in this dressing is examined after 48 hours it will be found that there is still active zinc peroxide present. In the perineal wound of an abdomino-perineal operation, or any deep cavity, it will remain moist and active for a much longer period of time. I have left it in a perineal wound for nine days without having it dry. Heating is advisable to sterilize it and activate it to its maximum efficiency, but the latest preparations are reasonably active without heating and may be used safely in badly infected wounds. The heated preparations do not deteriorate now, as they did formerly, and may be used as long as a year after activation.

We have been looking for a long time, however, for some medium in which the zinc peroxide would be active without drying, and have only recently found such a medium. Quite independently, Doctor Altemeier and I have both come to the use of the glycol preparations known as the "carbowaxes." Great interest in vehicles has recently been stimulated by the necessity for finding a suitable medium for the sulfonamide group of antiseptics, and the "carbowaxes" have been put forward as possibilities in this field. They represent a whole series of glycols varying in molecular weight and running all the way from thin liquids to dense solids. The liquids and solids may be mixed in appropriate proportions in order to give any desired consistency and melting point. The simpler ethylene glycols are toxic but triethylene glycol and the higher glycols are apparently nontoxic, and may be repeatedly injected into animals in large quantities without any harmful effects.

This is still in an experimental stage of development, and the ideal medium will be found, I believe, by further experimentation. Doctor Altemeier's study of the oxygen evolution of these various preparations and the hydrogen ion studies are very important in this development.

I fully agree with Doctor Altemeier that with any surgical infection there must

be a careful analysis of the active organisms and the appropriate treatment must be determined on the basis of this knowledge. Zinc peroxide is not only a bacteriostatic agent but bactericidal for the anerobic and micro-aerophilic organisms as well as for many of the aerobes, particularly the hemolytic streptococcus and other aerobes which are susceptible to peroxides. It also neutralizes, probably by oxidation, many toxins both bacterial and chemical. Among the latter are the poison ivy toxin and the irritating chemicals of mustard gas and lewisite. In addition, in the higher concentrations it is also bacteriostatic for such organisms as staphylococci and pyocyaneus. For its effective action, there must be close contact and if a wound has a considerable amount of slough this must be largely separated first. Dakin solution is the best means we now have of liquefying the slough. However, there are many limitations to its use which are too well known to mention here. It was hoped that urea could be depended upon to liquefy slough, but it delays wound healing and has other disadvantages.

I want to congratulate Doctor Altemeier on the work he has done in this field, and I hope that others will follow the investigations both in the laboratory and in the clinic.

Dr. William A. Altemeier (Cincinnati, Ohio, closing) : I wish to emphasize again that we believe zinc peroxide therapy should be limited to specifically indicated lesions and should not be used indiscriminately. We believe, too, that the intelligent use of Dakin's solution is still the most effective form of therapy for the average infected granulating wound seen by the surgeon.

ERRATUM

Traumatic Shock: An Experimental Study Including Evidence Against the Capillary Leakage Hypothesis. Jacob Fine, M.D., Arnold M. Seligman, M.D., and Howard A. Frank, M.D. Annals of Surgery, **118**, No. 2, 238–255, August, 1943

The name of Howard A. Frank, M.D. should be deleted as a co-author, and also removed from the running heading.

ADDENDUM

Liver Necrosis in Burns: F. W. Hartman, M.D., and H. L. Romence, M.D. Annals of Surgery, **118**, No. 3, 402–416, September, 1943.

The original manuscript of this article was received for publication in the Annals of Surgery, March 17, 1943, having first been submitted to the National Research Council on February 11, 1943. It had been scheduled to appear in the Annals of Surgery for May, 1943, but had to be deferred to the September issue because of paging limitations. The paper was read before the American Society of Clinical Pathologists, Chicago, June 5, 1943.

EXPERIENCES OF A SURGICAL CONSULTANT OF A SERVICE COMMAND*

COLONEL BRADLEY L. COLEY, M.C.

SURGICAL CONSULTANT EIGHTH SERVICE COMMAND

DALLAS, TEXAS

ABOUT A YEAR AGO the Surgeon General of the United States Army established a consultant service for the Service Commands comprised of staff of three medical officers qualified in medicine, surgery and neuropsychiatry. Their duties are to evaluate the professional qualifications of the medical personnel, appraise new therapeutic methods and agents and coordinate professional practice by local discussion with hospital staffs of such problems as may present themselves.

It has seemed of interest to present some facts regarding the scope of the activities of the surgical consultant to a Service Command, to show the manner in which he functions, and to discuss briefly some of the problems encountered and show how they are being met.

The various fields of medicine and surgery were assigned by the Surgeon General as follows:

MEDICINE: All medical specialties (except neuropsychiatry) venereal disease, dermatology, dietetics and clinical pathology.

SURGERY: All surgical specialties (including urology, otorhinolaryngology, radiology and physical therapy).

NEUROPSYCHIATRY: Neurology, psychiatry and war neuroses.

The following remarks will be principally confined to the field of surgery.

In order to understand the hospital problem in an army at war one should appreciate first of all the difficulties under which a new installation is set up. In times like the present, a hospital of one or two-thousand beds is created in a cotton field or cow pasture in a few months' time. Thereafter, a heterogeneous group of doctors, dentists, veterinarians, nurses, sanitary and medical administrative corps of officers are sent. With the help of a cadre of enlisted men and of civilian employees, the hospital must be placed in operation with the minimum of delay. This conglomerate group must not only learn their individual duties but learn how to function effectively as a unit.

The medical officers come from all sections of the country and have greatly divergent viewpoints and varying degrees of training. It would ordinarily take considerable time to complete this integration, yet time is so essential that the hospital must begin to receive patients before it is fully accomplished, and when patients are received they must be given adequate care immediately. This coordination of the professional services is among the most important of the consultant's duties.

* Read before the American Surgical Association, May 13–14, 1943, Cincinnati, Ohio.

OBJECTIVES OF A SURGICAL CONSULTANT

The objectives of the surgical consultant are varied but they all have but a single purpose—to provide the best possible care of the sick or wounded soldier. All other aims are subordinate.

The policy has been to carry out this objective by having the Consultant make and maintain intimate contact with the services of the medical installations in the Service Command. The aim has been to correlate the various sections with the service as a whole and that of the services with one another; to assure the hospitals as even a distribution of qualified specialists as possible; to encourage and advise the officers in better performance of their duties and to raise as far as possible the standard of professional care by means of postgraduate education. There is a general agreement among us in the Service Command that the standard of professional care is no better than the educational level of its medical officers. We are unanimous in the feeling that the type of graduate education best adapted to our needs is that which is brought to the hospital. This enables us to reach the whole staff, including the younger medical officers who should after all be our chief concern. By contact with distinguished civilian or army doctors they can learn by doing. We shall obtain funds from one of the foundations to carry out such a program which will include such features as:

a. The institution of weekly clinicopathologic conferences.

b. The introduction of clinical case teaching in psychiatry.

c. Encouraging the establishment of bimonthly Journal club meetings for the express purpose of reviewing the current medical literature.

d. Weekly meetings of the major services.

e. Monthly staff meetings.

f. Grand ward rounds.

g. Inviting nationally known internists, surgeons, psychiatrists, pathologists and radiologists to visit the larger medical installations for a day or two. The invited guests will make ward rounds, hold clinics, give demonstrations, *etc*.

ACTIVITIES OF A SURGICAL CONSULTANT

The surgical consultant's sphere in relation to the civilian hospital is clearly understood by all of you. He has attained that position by virtue of his years of experience in his chosen field which was often gained in the hospital he now serves as consultant. He is familiar with its professional and administrative components. In the army, however, his activities necessarily differ considerably. He is not merely called upon to assist in the diagnosis or treatment of a specific case. Indeed, this is a small and relatively unimportant part of his function.

The major duties of a surgical consultant to a Service Command center about his visits to the hospitals. His value lies in his ability to acquire an intimate knowledge of the men on the surgical services and to appreciate

their individual problems. Effort should be made to harmonize the methods of treatment with established Army procedure, yet without destroying initiative or interfering unnecessarily with the independent action of the Chief of the Service and his section chiefs.

He should study methods in use and, by observing the results of trial of experimental procedures, he can evaluate them and pass the information along from one camp to another through the medium of the Service Command or by word of mouth. He is a sort of circuit rider who picks up ideas and methods and distributes them from one to another.

He must assist the personnel officer in every possible way to the end that the spread of surgical officers be as even as possible, that deficiencies of personnel are corrected and that the most efficient use is made of the supply of trained surgeons. There has been some recent criticism by members of teaching institutions of the policies of the Army in selecting men for medical officers. In all probability the magnitude of the task of furnishing competent medical officers, not only for all the fixed hospitals but for countless units for overseas service, is not generally appreciated by civilian doctors. Already, many men have been transferred to these units and the staffs of our fixed hospitals have not been receiving comparable replacements. It is foreseen that in the months to come there will be an increasing need for economies of surgical personnel. Already an effort is being made to train an officer as an understudy for each important position on the surgical service. Methods are being explored that will lift some of the administrative burdens that diminish the available time and energy that might otherwise be spent in purely professional activities.

RELATION OF THE SURGEON TO THE TRAINING PROGRAM

The surgeon is concerned with the care of the soldier from the time he arrives, still a civilian, at an induction station until he is discharged from the army. Let us consider the various stages at which our contact with him takes place.

The induction station is not only the first but also perhaps the most important. For here is the first and most effective point at which the physically unfit should be weeded out. It is regrettable that the induction station examination fails to eliminate so many men who are destined later to be separated from the service.

To anyone who has observed men at the induction station and during their training program, it is an unescapable fact that the physical condition of the youth of this country is not what it should be. Colonel Leonard Rowntree has pointed this out in a recent interview with a prominent sports editor. He stated that one out of four of the 17- and 18-year-old group is rejected on physical grounds, while in Sweden the rate is but one in ten. The need for a more intensive effort to provide our boys in school and college with better body building and physical toughening should be more generally appreciated and steps taken on a large scale to improve this situation.

The next, and also very important, place where screening takes place is at the Reception Center. Here, too, the great bulk of selectees who have defects or physical limitations that prevent their being of use to the army are weeded out.

The Replacement Training Center, where the recruit undergoes his basic training, is also a point at which further elimination occurs. This is the first stage at which the ability of the soldier to stand-up against the rigors of training is put to the test. Here the foot disabilities, the knee and back conditions, the overlooked herniae and pilonidal cysts begin to present themselves. Before the basic training has progressed very far the vast majority of defects that are destined to disqualify should have been noted; and the sooner they are discovered the better for the Army and for all concerned.

Considering the physical condition of the average inductee, the training program is certainly strenuous. The long hikes with full pack; the obstacle course and the other measures for toughening the soldier are responsible for bringing to light many latent physical defects and for many accidents.

Upon completion of basic training the soldier is assigned to a tactical unit and from there on he is subject to the injuries and accidents common to the branch to which he is attached. The types of trauma sustained bear a direct relationship to the training program he is undergoing.

From the time a soldier arrives at the Reception Center until he reaches a staging area to be sent overseas, the station hospital bears the brunt of his medical and surgical care.

The camp dispensaries serve as counterpart in the Army of the doctor's office or the outpatient department of a civilian hospital. It is here that the soldier reports for sick call; is examined by the medical officer and, if his condition warrants it, is sent directly to the station hospital. The dispensary, therefore, fills an essential function. It acts as a dam to hold back the flood of potential admissions to the hospitals which without it would be overwhelmed by a host of patients with minor ailments. The dispensary also makes it possible to keep more men on duty, lessens the ineffective rate and thus speeds the training program. A man who can be kept out of the hospital without harm to himself is far better off. The trend is definitely toward treating on a duty status all minor conditions in which hospital care is not actually needed. It is, therefore, important for the surgical consultant to visit these dispensaries and to assure himself that they are fulfilling their proper function.

GENERAL HOSPITALS

When the soldier completes his training and is ready for overseas service, he is sent to a staging area and there he passes out of our sphere. However, when he returns as a casualty he is sent to a general hospital where his care again becomes our concern. Just as the station hospital provides for all the ordinary professional care, the relief of uncomplicated surgical conditions, so the general hospital serves as a "medical center" in civilian

life. Here the professional attainments of the staff are expected to be of the highest, the facilities for diagnosis of obscure conditions of the best, and the opportunity exists for prolonged care of cases that require it.

There is a growing scarcity of highly-trained and qualified surgeons for positions of responsibility in the general hospitals. As a consequence, in some of these hospitals, the level is somewhat below the desired standard. In others, there is a lack of qualified specialists in such fields as neurosurgery, plastic surgery and thoracic surgery. The correction of these deficiencies is one of the consultant's chief concerns.

SURGICAL CONDITIONS COMMONLY ENCOUNTERED

While examples of almost every conceivable variety of surgical conditions are encountered, the vast majority are of two types:

a. Conditions commonly seen in young adult males, unrelated to Army service.

b. Accidents or injuries due to the training program. In addition, there are the usual mishaps sustained by the soldier on leave or on pass.

Under the first category we see many cases of hernia, appendicitis, varicose veins, hemorrhoids, pilonidal cyst, and such orthopedic conditions as torn or loose semilunar cartilages, static foot disabilities, recurrent shoulder dislocations and disturbed function due to old fractures and dislocations.

In the second we find many severe sprains, all types of fractures, including ankle and wrist, and a surprising number of fatigue or march fractures of the metatarsal, accidental bullet wounds, and severe head injuries. Burns have not been frequent. Trauma serious enough to require immediate or subsequent amputation is not uncommon. The nature of the injuries and their severity differ according to the type of training that pertains to each camp. For example, the skeletal injuries have been severe and a good many have been fatal in camps where antitank and commando training or tank unit training is given. In Air Force hospitals the few fractures seen are generally severe.

Anticipating the fact that certain diseases and injuries will require surgical treatment in which a high degree of specialization is necessary, the Surgeon General has designated certain general hospitals for this purpose. For example, to give the name of one hospital in each category, Brooke General Hospital for neurosurgery; McCloskey General Hospital, an amputation center; Walter Reed General Hospital, maxillofacial and plastic surgery; Letterman General Hospital, ophthalmic surgery and treatment of blinded casualties; and Fitzsimmons General Hospital, chest surgery. When casualties from overseas begin to arrive in large numbers the activities of the general hospitals will be greatly accelerated.

THE ARMY VIEWPOINT IN SURGICAL DECISIONS

While in most respects the viewpoint of the civilian and the Army

surgeon coincides, there are certain instances in which they must of necessity differ. The aim of the surgeon in civilian practice is to provide care of the patient and his interests are the only ones concerned.

In the Army, however, the principal objective of the surgeon is to increase as far as possible the number of effective man-days. In general, these two aims coincide and yet there are numerous situations that arise in which the needs of the Army make it insistent that the latter take precedence. Thus, when defects are discovered that obviously existed prior to entry into service, the surgeon must decide whether their correction in the Army is justified or whether discharge from service is a better solution. In reaching this decision he must consider whether after the operation the man is likely to make a satisfactory soldier. This demands an appraisal of him as a whole and may require the assistance of a neuropsychiatric consultation. Then, too, the gravity of the operation, the risk of complications or sequelae, and the probable end-result must be weighed in each individual case. It is here that the medical officer fresh from civilian practice is at a disadvantage at first and must learn by experience how to evaluate these factors to the ultimate advantage of the Army.

Operative procedures that require prolonged dressings or extended convalescence, such as the open packing method of handling cases of pilonidal cysts are not acceptable in the Army because in most camps a man must be on "full duty" or in hospital; there is no such thing as "light duty." During the first nine months of 1942, this Service Command had 780 admissions of pilonidal cyst cases to its hospitals. They were responsible for more than 29,000 man-days lost to the training program.

These considerations only apply to elective surgery for conditions existing prior to induction. Where a man develops a disease or sustains an injury while in service and it is clear that it is not related to a preexisting defect, the same general considerations obtain as in civil life, and no form of surgical treatment is withheld that promises the most complete cure or restoration of maximal function.

SURGICAL TECHNIC IN ARMY HOSPITALS

The surgeons and specialists attached to the surgical service of station and general hospitals are men who have, until recently, been engaged in civilian practice. Their technic, therefore, is about what one would expect to find in any first-class civilian hospital, the variations in technic reflect the differences to which their previous training has accustomed them.

There is a general regard for the observance of measures to maintain sterility in the operating room. Preparation of the hands, careful masking of all operating personnel, skin preparation, and exclusion of skin by prompt application of towels to the wound edges, are all matters that are given proper consideration. Care and gentleness in handling tissues, avoidance of blunt dissection and rough retraction and general puttering while operating, are all given attention. While the use of nonabsorbable ligature and suture ma-

terials is much more widespread than was anticipated, there are still many surgeons who adhere to chromic catgut. There is, however, a noticeable tendency to use it in finer caliber and to insist on meticulous hemostasis and to avoid placing sutures under tension. This is, of course, very gratifying, for it undoubtedly reflects a growing appreciation of the advantages that accrue when so-called "silk technic" with all its implications is adopted. Alloy steel wire is used by a few surgeons who appear well satisfied with results obtained.

The local use of sulfonamides in wounds made by the surgeon varies greatly in the different hospitals. It is probable that it is used more frequently than is strictly indicated and that its daily use on granulating areas that are not grossly infected is unwarranted, and may have a tendency to retard wound healing. In this connection, there is also an inclination to give sulfonamide drugs internally in cases of mild superficial infection, without waiting to see the effect of local measures, such as heat and wet dressings, elevation and physiologic rest of the part. Before the advent of these drugs such treatment was generally promptly effective. There is evidence in recent medical literature that in a considerable percentage of cases reactions follow the use of sulfa drugs in patients who have previously been given them. It seems advisable, therefore, not to use them in mild infectious processes until the beneficial effect of other measures has been tried.

SUMMARY

The activities of a surgical consultant to a Service Command and some of the problems encountered and observations made have been briefly presented.

The quality of the inductees has been disappointing both as to their specific musculoskeletal defects and their general physical development and stamina. The need is apparent for a more adequate nation-wide program to correct this situation and provide more robust and tougher youths.

Surgical technic and the general care of surgical patients are found, for the most part, to be of a high order. Whether or not the expected depletion of the supply of well-qualified surgeons results in a lowering of the standard now existing depends on how successfully we compensate for it by increasing the effectiveness of the surgeons we have.

In closing, let me assure you that the surgical profession need have no fear that the men who are carrying the load in our Army hospitals will fall short of previous high tradition. They are giving conscientious service, their judgment and technic are excellent, and their hearts are in this job.

DISCUSSION.—COLONEL GROVER C. PENBERTHY: Colonel Coley has covered the subject very completely in his brief presentation. The contribution of the War Department, through the efforts of the Surgeon General, in establishing this consultant service is to be commended. The consultation service, as it applies to the care of the soldier, is helping indirectly to reduce the period of morbidity, the hospital days, and disposing of the individual soldier that will not become a good soldier.

In going about and visiting the hospitals, I am impressed, as Colonel Coley has

emphasized, with the high caliber of young officers that are leading the way in the teaching program as well as the technical work in the hospitals. These young men who have had good internships and others who have had a residency, are leading the way and doing a very constructive job.

In regard to the training program. This will vary in some of the hospitals, but with the individual officer who has been associated with a teaching institution, the postgraduate program of teaching is excellent. Each officer is expected to contribute. In the ward walks, the clinical pathologic conferences, and the various meetings of the journal clubs that I have attended, I am impressed with the sincere desire of the officers to acquaint themselves with the Army method of treatment and the proper disposition of patients.

Relative to the responsibility of the consultant in reference to the training and the selection of qualified officers, we try to evaluate each officer from the standpoint of his interest in a particular subject. The Surgeon General, in establishing courses that are carried on in civilian institutions, certainly has added to the interest and morale of the young men. They are desirous of attending these courses, and I, for one, appreciate the interest that the civilian physicians and surgeons are taking in the officers that have been assigned.

Unfortunately, we can not always assign the officers that make application, but if the courses are to be continued, and I understand that they are, in due time we may have an opportunity of recommending some who may still be on duty in the United States.

In closing, I want to congratulate Colonel Coley on his approach to this responsibility entrusted to the consultants. He has covered the field thoroughly, and I am sure that the experiences in the Fourth, Fifth, and Ninth Service Commands will run parallel to those of Colonel Coley in the Eighth Service Command.

CAPTAIN WALTMAN WALTERS, M.C., U.S.N.R. (Corona, Calif.): I recently had the pleasure of accompanying Colonels Coley and Penberthy, and Lieut. Col. Griswold on some of their inspections to various United States Army hospitals. I can concur in the statements which they have made, and I think members of the American Surgical Association, who have had an opportunity to visit some of the Army or the Naval hospitals, would be equally pleased to see the very fine type of medical and surgical practice which is being carried out in them. One does not need to wonder at it, when one realizes that the supervision and the consultation of the surgical services are under men of the type whom I have mentioned, who are members of this Association and who, I might say, are directly responsible for the character of the surgical work in those hospitals. I do not think we need to worry about the type of surgical treatment which the soldiers and sailors are receiving in the Army and Navy hospitals.

A word about the Naval hospitals. We have a little different system of medical and surgical consultation and supervision. The President of the United States appointed a group of honorary consultants—on recommendation of Admiral McIntire, the Surgeon General. Among them Doctors Lahey, Balfour, Dandy, Wiener, Lowsley, and the late Doctor Crile—Admiral McIntire has had them visit and inspect the naval hospitals. That does not mean just a cursory examination of the physical properties of the hospital. It means an examination of patients, of records, of medical and surgical personnel, *etc.*

In addition, you might be interested to know that in the Naval hospitals a monthly report of patients, their diagnosis and disposition is obligatory on the part of the commanding officer, which is made out and sent to the District Medical Officer, who, in turn, sends it to the Surgeon General of the Navy. Almost without exception postmortem examinations are routinely obtained.

Now about the methods of receiving information on the advances in medicine and surgery. The Navy has a medical bulletin,* which is published bimonthly, which contains much of the latest and more recent important work in military or Naval medicine. In addition, Navy Medical Officers receive a bulletin every second week from the

* United States Naval Medical Bulletin.

Bureau of Medicine and Surgery,† in which are reports of the researches of chemical investigation by Naval and civilian doctors, and reports from the Committee of Surgery of the National Research Council. The work of the National Research Council in furnishing the Medical Corps of the Navy and the Army with this very important information, a part of which you have heard today, has helped to improve the treatment which Naval patients are receiving.

At the Naval hospital at which I have been stationed for about a year, we have two staff medical meetings a week, one in which we show moving pictures of various types of operative procedures, with the presentation of a medical paper by alternating members of the staff. At the second meeting abstracts and reviews of the medical and surgical literature are presented.

There are several Army installations around us, and the Army medical officers attend our medical meetings and we theirs. Further evidences of collaboration between the medical officers of the Army and the Navy is the report that after the Naval and Marine casualties were taken care of at Guadalcanal and evacuated, some of them were sent to an Army hospital based on one of the islands in that group, and to Naval medical hospitals based on other islands there were many Army patients in addition to those from the Navy.

I have enjoyed Colonel Coley's paper very much. I enjoyed being with him on some collateral duties, as well as with the other men I have mentioned, and I think it is a credit to the Army Medical Corp that they have asked men of that type to serve as consultants and advisers.

Colonel Bradley L. Coley, M.C. (closing): I would like to say a word about graduate medical education as we conceive of it in the hospitals of a Service Command. We believe that efforts to provide every facility which may aid in elevating the level of medical practice in Army hospitals is one of our most important obligations. Towards this end, we have instituted a program which will embody the following: Experimentation with libraries, in order to determine what constitutes the smallest acceptable library which will give definitive information concerning all types of medical and surgical cases; instituting clinicopathologic conferences of the type used at Massachusetts General Hospital; and inviting nationally known specialists in the major fields of medicine and surgery with the express purpose of their participating in an informal way in all the activities of the station hospitals during their stay.

In closing, I would like to urge the members of this Association, who may play a part in shaping the courses of War-Time Graduate Medical Education, to consider, insofar as Army Hospitals are concerned, the desirability of emphasizing the direct contact, on an informal plane, between the teacher and the medical officer. It has seemed to us that by this method, which involves grand rounds, attendance at clinical conferences and free discussion of actual clinical problems arising in each individual hospital, more is accomplished than by formal lecture courses from the rostrum.

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†Bumed News Letter (Navy Dept.). (Abv. for "Bu. Med. & Surg."—The term "Bumed" is correct.—S.T.P.)

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